



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

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OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

Honorable Michael O. Leavitt
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Clean Air Scientific Advisory Committee (CASAC) Particulate Matter (PM) Review Panel's Review of the Agency's *Fourth External Review Draft of Air Quality Criteria for Particulate Matter (June 2003)*

Dear Administrator Leavitt:

EPA's Clean Air Scientific Advisory Committee (CASAC), supplemented by expert consultants — collectively referred to as the CASAC Particulate Matter (PM) Review Panel ("Panel") — met on August 25-26, to review the two-volume, June 2003 draft document, *Fourth External Review Draft EPA Air Quality Criteria for Particulate Matter* (EPA/600/P-99/002, aD, bD) in a public meeting held at the EPA facility in Research Triangle Park, NC. This was the fourth CASAC review of the draft Air Quality Criteria Document (AQCD) for PM in the current cycle for reviewing the National Ambient Air Quality Standards (NAAQS) for PM. The CASAC was established under section 109(d)(2) of the Clean Air Act (42 U.S.C. 7409) as an independent scientific advisory committee, in part to provide advice, information and recommendations on the scientific and technical aspects of issues related to air quality criteria and NAAQS under sections 108 and 109 of the Act. As noted below, the CASAC PM Review Panel felt that this version of the draft document, while substantially improved over the Third External Review Draft, required additional revisions — to include a completely rewritten integrative synthesis (Chapter 9) — before it could be deemed to represent an acceptable summary of the current science on particulate matter.

1. Background

EPA is in the process of updating, and revising where appropriate, the AQCD for PM as issued in 1996. Section 109(d)(1) of the Clean Air Act (CAA) requires that EPA carry out a periodic review and revision, where appropriate, of the air quality criteria and the NAAQS for "criteria" air pollutants such as PM.

The CASAC PM Review Panel reviewed the October 1999 First External Review Draft of the AQCD for PM in December 1999, focusing primarily on the organization, structure, and presentation of material in the draft document. This was an early, incomplete draft of the PM AQCD, and it was understood that additional information would be incorporated in subsequent drafts. Accordingly, there was no expectation that the Panel would close on the draft document at this stage of its development. Nevertheless, the Panel was generally complimentary about the content and quality of this draft AQCD, while noting the need for considerable development both in structure and content.

The Agency revised the document in response to CASAC PM Review Panel and public comments, as well as to reflect additional new studies on PM effects that were not available in time to be referenced in the First External Review Draft. In July 2001, the Panel met again in a public meeting to review the March 2001 draft document, *Air Quality Criteria for Particulate Matter – Second External Review Draft*. Despite the fact that this version of the document was substantially revised and expanded, the Panel could not come to closure on that draft document and requested that the Agency further revise the draft PM AQCD.

EPA again revised the document in response to comments from the Panel and the public, and to reflect more new PM studies that had become available. The CASAC PM Review Panel met again in a public meeting in July 2002 to review the two-volume, April 2002 Third External Review Draft of the AQCD for PM. Following that third CASAC meeting, EPA again revised the document in response to CASAC PM Review Panel and public comments, and also to take into account peer-reviewed analyses of a number of epidemiological studies conducted to address statistical modeling issues that were identified after release of the latest draft PM AQCD.

On June 30, 2003, the Agency made available for public review and comment a Fourth External Review Draft of the revised AQCD for PM.

2. CASAC PM Review Panel's Review of the *EPA Air Quality Criteria for Particulate Matter (Fourth External Review Draft)*

While the CASAC PM Panel generally found the Fourth Draft of the Air Quality Criteria Document for Particulate Matter to be substantially improved over the prior version of the draft document that had been reviewed in July 2002, it was felt that the draft required additional revisions before it could be considered as an acceptable summary of the current science on PM and provide the appropriate scientific foundation for the Staff Paper. However, the Panel was able to come to agreement on a number of the individual chapters and has provided guidance on the remaining chapters. The most significant deficiencies were in the integrative synthesis chapter (Chapter 9).

The CASAC PM Review Panel would like to commend the Agency, and particularly the staff of the National Center for Environmental Assessment (NCEA), within EPA's Office of Research and Development (ORD), for their effective and efficient treatment of the statistical problems that were identified last year in some of the epidemiology studies that were important

parts of Chapter 8. The Panel would also like to express their sincere gratitude to the Health Effects Institute (HEI) and their Peer Review Panel for assisting in a timely review of the reports of the reanalyses with revised statistical approaches. The development of HEI Report, *Revised Analyses of Time-Series Studies of Air Pollution and Health* (May 2003), greatly aided EPA in revising the criteria document. Finally, the Panel would like to thank all of the researchers who promptly reanalyzed their data once the full nature of the statistical problems became clear. A considerable amount of work was performed in a relatively short time, and the entire process permits the Panel to move forward with increased confidence that the PM air quality criteria document is appropriately summarizing the current state of the science on time-series analyses.

The remainder of this report will provide a chapter-by-chapter assessment of the Fourth External Review Draft PM air quality criteria document and the consensus views of the required changes. In addition, the members of the Panel have provided individual comments that are compiled in the appendices to this report and have been provided to the NCEA staff to aid them in the revision process.

The only concern with respect to Chapter 1 is that it does not clearly articulate the basic requirements for standard-setting, including the indicator, concentration, averaging time, and statistical form of the standard. Such discussion will focus the reader on some of the key issues that ultimately need to be addressed by the Agency's Office of Air Quality Planning and Standards (OAQPS) based in part on the scientific understanding of PM as represented in the air quality criteria document. The panel closed on this chapter given that these editorial changes will be incorporated into a final version of the AQCD.

There were no major remaining concerns with Chapter 2, although a number of minor corrections and comments are provided by the individual panel members in the material in the appendices.

In Chapter 3, a new approach to the estimation of "background" was provided. The Panel continues to express concerns regarding the problem of estimating the concentrations of pollutants that are advected into the atmosphere of North America and provide a lower limit on the concentrations that can be effectively managed. However, after discussion, the Panel agreed that the approach presented was reasonable and could serve as a good basis for making such estimations as were likely to be possible at this time. However, it should be recognized that any such estimate has a very high degree of uncertainty. While there were minor corrections and comments provided in the individual comments, Chapter 3 is considered closed with the expectation that these corrections will be incorporated into the final document.

In Chapter 4, there have been considerable improvements in the sections on ecosystem impacts, climate change and valuation of welfare effects. However, the chapter could be further improved to be more consistent with the other chapters in terms of clearly providing information necessary to estimate the risks of PM exposure at or near ambient levels. There remain concerns about the visibility section in which a number of inconsistencies were identified in the review of the Third External Review Draft, but have not yet been fully addressed. One of the best

understood relationships is that the extinction coefficient is proportional to the mass concentration for a given particle mix. However, this fundamental understanding is not clearly presented. There is an inconsistency in the document in that optical measurements are reported as a means to estimate particulate mass concentrations, but it appears not to give credence to the use of mass measurements to estimate optical properties. Visibility in Class 1 areas are already dealt with in the Regional Haze rules process, but there remain visibility issues in other areas that were not addressed at all in this document. The Panel requests that NCEA staff review the individual comments on this topic in both this report as well as the report submitted last year summarizing our review of the previous draft version. However, the Panel felt it could close on this chapter based on the revisions already made and the additional modification that will be made in response to the comments provided as appendices to this report.

Chapter 5 has been very substantially improved, and NCEA is to be commended for the inclusion of an important section on the relevancy of exposure assessment to epidemiology and toxicology. While it could still be more concise and better focused, it does bring an important perspective requested by the Panel. The chapter in general and this section in particular could be improved with some careful editing to shorten and focus the discussions. However, the Panel did close on this chapter since the remaining issues outlined in the individual comments can be handled with straightforward editorial changes that will appear in the final document.

Chapter 6 has been greatly improved in the Fourth External Review Draft compared to the third draft. The authors have added material on the comparison of dosimetry in laboratory animals versus humans that assists in the interpretation of toxicological effects and their potential relevance to effects in humans. In addition, detailed information has been added on regional and total respiratory tract deposition as a function of age for various particle sizes. However, the Panel found some technical errors in the presentation that will require careful revisions. The Panel agreed that an appropriate approach to resolve these issues was for CASAC Member Dr. Fred Miller to work directly with NCEA staff to ensure that the appropriate modifications were made. However, the Panel felt it could close on the Chapter subject to the usual minor revisions that will be needed to address the individual comments and suggestions that are provided in the appendices.

The Panel could not close on Chapter 7 because of a number of problems that have been identified. The authors of this chapter often strained to make the case for biologic plausibility despite the very high doses of particles used in comparison to real-world human exposures. Not as often do they state that caution is needed in interpreting the results for humans. The Panel urges the authors to achieve a better balance in the statements for support of the epidemiological results arising from some of the studies described in Chapter 7. In addition, the treatment of doses is very inconsistent across the chapter. Doses, or exposure concentrations and times, are given for some studies but not for others. Considering that toxicological information has very little value without explication of dose or exposure parameters, any study that is worth citing must be worth providing doses. This point has been raised repeatedly in previous reviews, and is still not dealt with satisfactorily.

Previously, CASAC has asked that various dose metrics be presented for human to rat ratios to facilitate interspecies extrapolation of the animal toxicology results. This could be done in the dosimetry chapter or in the toxicology chapter. One approach would be to use Table 4 from Dr. Miller (*Inhal. Toxicol.* 12: 19-57, 2000) as such a comparison that is in the literature. Alternatives could be acceptable, but something needs to be done to address this issue.

There remains some confusion in the chapter between exposures to diesel emissions and exposures to diesel particulate. Those are quite different exposures. Effects of exposures to whole diluted diesel emissions (or any other complex combustion emission) cannot be ascribed to the particulate phase unless some specific steps were taken to prove that it was the particulate phase and not the gas nor vapor phases that caused the effect. The particulate phase of diesel emissions comprises a very small portion of the total exposure to mass concentration of diesel emissions.

The issue of the presence of endotoxin in airborne particulate matter is not dealt with satisfactorily. It is discounted in some sections and highlighted in others. The *in vitro* section basically says that one of the NIST ambient PM samples, and many, if not most, of the other collected ambient PM samples contain endotoxin, and that endotoxin drives the cellular cytokine production. However, the summary of that same section doesn't even mention endotoxin. The overall summary in Section 7.7.1.8 notes that inhaled endotoxin has a threshold for "pulmonary and systemic" effects in healthy volunteers between 0.5 and 5.0 mg, and that ambient levels do not exceed 0.5 ng/m³. Of course, CAPs show a high threshold for effects in healthy volunteers as well, yet the document does not take that as an indication that ambient PM is not affecting people. Either endotoxin is an important component of ambient PM and the resulting health effects, or it is not. Either endotoxin is a sizable potential artifact in the toxicology information base, or it is not. There must be a consistent treatment of the issue and careful review and editing will be required. There is a potential serious problem if the chapter is saying that endotoxin is important for *in vitro* studies, but unimportant overall because those results can not be extrapolated to humans. If that is the case, then how can any extrapolation of other PM results from *in vitro* to humans be made?

The overall treatment of bioaerosols is extremely weak. It is imperative that the AQCD deal with at least airborne allergens in a meaningful way, as well as needing to mention other bioaerosols such as pollens and spores. Pollens and other allergens clearly exist in the particulate phase, and they certainly have public health importance (and are certainly "environmental"). It is clear to allergic people that airborne biological PM or PM-bound materials are important with respect to adverse health effects. The presence of allergens and other biological particles in the atmosphere is certainly part of the scientific understanding of the relationships between exposure to ambient particulate matter and health effects and has to be appropriately reflected in this chapter.

The "summary and conclusions" section at the end (Section 7.7) has major problems. It appears that this section was developed independently from the rest of the chapter. Very few of the subsections actually present a summary of the topic or present any high-level or "bottom

line” conclusions. Several of the subsections consist only of descriptions of individual studies. Even more problematic is that several of the subsections appear to describe studies that were not described at all in the body of the chapter. Obviously this is inappropriate in a summary and conclusions section. It is hard to integrate complex and disparate information into a limited number of overall conclusions than it is to simply list studies, but that is what is needed here as well as to feed into the integrative summary in Chapter 9. That need has not yet to be met.

Chapter 8 was not formally reviewed last year because of the concern over the statistical issues. However, the Panel felt that in general there was substantial improvement in Chapter 8. However, there are remaining problems that will need to be addressed.

It now appears that the chapter is not taking an advocacy position to convince the reader of a certain point of view, and there is a more balanced review and appraisal of the relevant literature. This Draft AQCD does do a better job of attaining the “goal of producing an objective appraisal of the evidence, including weighing of alternative views on controversial issues” (p.8-4, L8). More qualifiers are included when appropriate, and there is more indication that many findings are sensitive to modeling choices. For example, the relative effects of fine and coarse PM (pp.8.109-110 & 233) are presented with more objectivity, although there is still a tendency to attribute coarse PM effects to specific aspects of coarse PM composition. The description of the Lipfert cohort study is more fairly described (p.8-109 & 114), as is the section on harvesting (p.8-273). The conclusions regarding harvesting are appropriately conservative (p.8-273, L15). There is some unevenness of tone, possibly reflecting the patchy nature of the revisions, with some non-revised sections still maintaining the original stance. For example, the section on respiratory hospitalizations is not sufficiently balanced and the same problem remains with the section on heterogeneity of effects. A careful comprehensive editing of this chapter with attention to this issue should solve the problem.

With regard to the content of the chapter and the thread of argument to be used to present the epidemiological results, the Panel suggests that there be more a more explicit statement of what we think we know regarding air pollution and health effects. Particulate matter exists as a component of a complex pollution mixture that includes other criteria pollutants, as well as many other airborne contaminants that may convey risks to health. Particulate matter is of both primary and secondary origin, and two of the gaseous criteria pollutants (sulfur dioxide and nitrogen dioxide) contribute to the formation of secondary particles. Because of shared sources, concentrations of particulate matter, SO₂, and NO₂ may be correlated to a moderate degree in urban environments. Generally, concentrations of PM and other monitored pollutants are imperfect measures of personal exposures and the extent of measurement error likely varies among the pollutants and also among population subgroups. In interpreting the findings of multi-pollutant models, there are several alternative explanations for observed associations that need to be considered based on the points above:

1. An effect estimated for PM reflects a “true effect” of particulate matter (causal interpretation).

2. An effect estimated for PM reflects the total effect of the overall air pollution mixture (PM is an indicator of mixture toxicity).
3. An effect estimated for PM reflects confounding (at least to a degree) by another pollutant (PM effect is confounded).
4. An effect estimated for PM may be modified by levels of other pollutants (there is effect modification).
5. An effect estimated for PM may be an underestimate of the true effect because of the inclusion of other criteria air pollutants (SO₂ and NO₂ in particular) in a model which are contributors to the PM levels observed. This effect can be interpreted as the estimated effect of particulate matter on health not mediated by contributions to PM.

These alternatives are not clearly stated in the Air Quality Criteria Document. The AQCD would be advanced by a clear delineation of these relationships rather than the current general statements about residual confounding. There is always a potential for residual confounding, but raising the possibility does not advance interpretation of model findings.

We remain faced with the challenge of interpreting multi-pollutant models in an attempt to sort out the possibilities above. Further adding to the challenge is the problem of measurement error, which may be differential among the pollutants. The strength with which a causal interpretation should be advanced lies in how robust the short-term associations between PM and health outcomes are to alternative, plausible multi-pollutant models. Inclusion of other pollutants in models is “conservative” in a sense. At the least, such models take account of confounding by other pollutants to the extent possible and may lead to the underestimation of the effect of PM by inclusion of pollutants which are sources of secondary particles on the relative risk scale. These models do not address effect modification, which has been variably explored across studies.

In its exhaustive listing of the evidence, the database of this version of the draft AQCD affords some opportunity for judgment, informed by the framework laid-out above. The most informative data display would compare estimates from PM-only models with models adjusted for other pollutants, within studies as available or across studies. The HEI-funded National Morbidity, Mortality and Air Pollution Study (NMMAPS) offers such comparisons, for example. While residual confounding may always be advanced, a resistant PM effect across studies and outcomes, with control for other pollutants (and weather), is strong evidence against this possibility. Of course, we cannot rely on epidemiological studies alone to sort out the possibilities listed above and causal interpretation has always been based on the full scope of evidence. That is a topic to be covered in the integrated synthesis chapter.

It is argued that some gaseous pollutants might be considered to be part of the causal pathway in which PM causes adverse effects, and should therefore not be considered confounders. If this were true, then the gases should correctly not be included in PM models. A pathway for formation of PM is presented (p.8-204, L28) in which NO forms NO₂, which in turn forms nitrate, and contributes to the formation of organic fine particles through the

photochemical reaction sequence, which then contributes to the PM mass. This implies that the only effect of the gases (in this case NO₂) is through the formation of PM. Since the effects of the gases on health do not require that they act through this pathway, this argument does not hold up to scrutiny. Thus, this discussion needs to be clarified so that the direct effects of gaseous pollutants is properly included.

There is some inconsistency in how the role of gaseous pollutants in a given study is presented. An argument is made (see above) that the gases should not be considered as confounders. However, in many later presentations of PM effects and their sensitivity, or lack of sensitivity, to inclusion of gaseous co-pollutants in the models, this issue is not consistently addressed. Especially in the section reviewing morbidity effects, findings are presented from models in which variables for gases are typically included in the models to address the matter of confounding by the gases.

The issues regarding the impact of use of the default convergence criterion in Generalized additive models (GAMs) have been reasonably well-handled. There seems to be an implicit assumption (p.8-9) that estimates of effect from those studies that had not used GAMs are unbiased. It should be pointed out that, although these studies were not plagued by poor estimate convergence, effect estimates from these studies may be as sensitive to degree of temporal smoothing and specification of weather as any study that used GAMs.

There does not appear to be any general review, however brief, in the text of new/revised findings of single-city studies. There is a brief introductory section (8.2.2.2, p.8-23), and a section devoted to the new multi-city studies (section 8.2.2.3, p.8-30), but nothing about any general impact of the single-city studies, apart from listing them in Table 8-1. A brief discussion of their contribution to the weight-of-the-evidence should be included.

The presentation and discussion of studies of chronic PM effects is reasonably balanced and indicates issues, such as that of spatial correlations (p.8-86), that are not fully resolved, and model sensitivities, such as sensitivity to inclusion of time-dependent PM measures. One aspect of spatial correlation that is confusing, is the relationship between spatial correlation and confounding. There is a suggestion in the AQCD that accounting for spatial correlation will address potential confounding due to unmeasured factors that are spatially related to pollution and mortality (see p.8-95, line19 [section 3, 2nd sentence], for example). It is not clear that is true, in the same way that accounting for autocorrelation in time-series studies does not address confounding due to time-varying confounders. Therefore, while accounting for spatial correlation is important, adequately accounting for it does not provide assurance that effect estimates are unconfounded. There is also the problem of reporting only “best lags.” There has been literature on this issue, particularly the work of Lumley and Sheppard (p.8-234) that provided clear guidance on this issue. When best lags are used to indicate the range of estimated effects, such as in Figure 8-12 (p.8-137) for cardiovascular hospitalizations, and when “the maximum lag model” (p.8-149, L14) is used for estimating range of effects for respiratory hospitalization, the range is biased upwards. The statement, “While this practice [use of best lag] may bias the chance of finding a significant association, without a firm biological reason to

establish a fixed pre-determined lag, it appears reasonable” (p.8-234, L15). It is not reasonable to use effect estimates known to be biased and thus, should not be presented in this manner. While it is true that there is often no good biological reason for preferring one individual lag over another, this in no way supports use of a biased effect estimate.

Another example that demonstrates an unfortunate tendency to selective summarization of results pertains to the conclusion that the results of the reanalyses of respiratory hospitalizations did not substantially affect conclusions. Zanobetti and Schwartz (2003) reported revised findings on pneumonia hospitalizations from the 14-city study. Tables 8-17 (p.8-150) and 8-18 (p.8-152) give the impression that effects were still present, even using generalized linear model (GLM) and natural cubic splines. Unfortunately, this effect is only present for lag 0 or the mean of lags 0 and 1; for all other lag formulations, including the distributed lag, arguably a preferred formulation, the previous effects disappeared (see p. 51 of the HEI Special Report, *Revised Analyses of Time-Series Studies of Air Pollution and Health*, May 2003). At the least, these findings indicate extreme sensitivity of the pneumonia findings to approaches to smoothing. Such selective presentation tends to weaken the overall impression that this version of the chapter is more objective and balanced than previous versions.

The document states: “The time-series studies published since 1996 have all controlled adequately for weather influences” (p.8-146, L18). Members of the Panel questioned this. Concern remains as to how to control for meteorology and other time related potentially confounding factors. The sensitivity of findings to weather specification is again an active area of work. As evidence that the debate over the correct specification of meteorology continues, an attempt is made to attribute the smaller effect estimates from NMMAPS to mis-specification of meteorology effects (p.8-48-49). It is perhaps equally likely that larger effect estimates from other multi-city studies are due to mis-specification of meteorology in those studies. The principal point for interpretation is the sensitivity of the findings to alternative specification of the meteorology in the models.

While this discussion (section 8.3.2.5, p.8-165) is generally well done, it should be noted that studies addressing susceptible subgroups seldom include a direct comparison among different subgroups within a single study, and therefore do not directly address the issue of susceptibility. Therefore, statements such as, “...the elderly are especially affected by air pollution” (p.8-166, L9) and “The groups identified in these morbidity studies as most strongly affected by PM air pollution are older adults and the very young” (p.8-168, L5) need to be weakened.

There is a terminology question with respect to “intervention” studies. The text discusses “interventions,” referring to examples of “natural experiments” in which step changes in PM concentrations have occurred. These studies are not interventions in the experimental sense, but rather represent examples of “found experiments.” The advantage of such changes in exposure is the decoupling of change in exposure from factors that might be confounding its effect. There is an opportunity to strengthen causal inference as a result.

There remains the problem of criteria for including more recently-published papers. There are several including the paper by Hoek *et al.* on Dutch mortality since it was already mentioned in Chapter 5 and provides a link between exposure and adverse effects. It may be that papers that help clarify cross-chapter issues are the ones that rise to the level of inclusion. Some important recent “intervention” studies, notably the Dublin and Hong Kong mortality studies, were not included. This is unfortunate, since these have direct relevance to the PM AQCD, and like most “intervention” studies, avoid some of the weaknesses of the other types of observational studies reviewed. The Panel questions the strength of the statement, “Taken together, these epidemiologic intervention studies tend to support the conclusion that reductions in ambient air pollution (especially PM) exposures resulted in decreased respiratory and cardiovascular health effects” (p.8-218, L11). For Atlanta, a primary role for ozone is as likely as that for PM, and for East Germany and especially Hong Kong, the evidence is more compelling for a role for SO₂ than for PM. However, the sum of data from toxicology, aerometrics, and human studies would suggest that SO₂ may be acting as a surrogate for PM.

Regarding the “intervention” studies that are reviewed, it appears that the summary of the Utah steel mill closure studies is incorrect and needs to be changed (p. 8-214, L24). Only the published study of monthly hospitalizations used the period of steel mill closure in the design and analysis. The study of mortality, lung function, symptoms, and school absenteeism used traditional time series or longitudinal panel study designs to evaluate daily effects of short-term changes in PM concentrations, and did not explicitly investigate the effect of the steel mill closure. The summary in the AQCD indicates that all of these health outcomes were part of the “intervention” study, when in fact they were not.

The discussion of heterogeneity of effect estimates in NMMAPS is misleading, and sometimes incorrect. Further inspection of the plots derived from NMMAPS in which city-specific effect estimates are ranked by a measure of power in the so-called “funnel” plots (pp.8-244, 245), show little evidence to support the contention that cities with higher power tend to show consistently positive estimates of effect. In fact, of the eight cities with the most power, two show no effect (one slightly negative), three are substantially below the already low mean estimate of effect, two are just below this average, and one (New York City) is substantially higher than the average. It is hard to find a consistent message there. Obviously the precision of the estimates narrow as power increases, but a figure isn’t necessary to make that point. It is incorrect to state that “many [effect estimates are] statistically significant” (p.8-243, L27; p.8-246, L4 & L10), since only that for New York City and Oakland, of all the 90 cities, is positive and statistically significant. Further, the impression of objectivity is hampered by drawing particular attention to the estimate of effect for Oakland (Fig. 8-22, p.8-245, L11) in the group of “Northwest” cities, just because it happens to be larger than effects of the other cities with high power; 4 cities in the Northwest have greater power than Oakland. The characterization of effects for industrial mid-west cities with the most power as “positive” (p.8-246, L4), while strictly true, is nevertheless misleading when one views the figure (Fig. 8-22), since effect estimates of four of the five cities with the most power are very small, and obviously not significant. The characterization of effects of cities with the most power in the “upper mid-west” and the southeast as tending “to be positive and not far off the nationwide mean” (p.8-246, L18-

19) is also misleading, since for the “upper mid-west”, two of the top three show either no effect or are negative, whereas for the southeast, two of the top four are negative (Fig. 8-23, p.8-245).

The issue of heterogeneity is important. One does not find a clear discussion of the fact that a statistical test for homogeneity of effects in the revised NMMAPS failed to reject, prompting the investigators to conclude that there was no statistical evidence for heterogeneity of effect. However, the power of this test to detect heterogeneity is low, given even less precision in the city-specific effect estimates in the revised analyses. The issue of heterogeneity of effect is still therefore a very open question.

The statement that low effect estimates in NMMAPS tended to be seen in cities with lower PM10 concentrations (p.8-246, L26) is also incorrect. In fact, the opposite is true. When the NMMAPS investigators explored city-level factors that might relate to PM effect estimates, mean PM concentration tended to be negatively associated with the PM effect estimate, indicating that cities with lower PM concentrations had higher estimates of PM effect, and vice versa.

The discussion of the role of measurement error (p.8-250, etc.) is generally well done, and emphasizes the important distinction between total personal PM and personal PM of ambient origin. The issue as to whether measurement error can account for the potentially falsely negative estimates of coarse PM effect is not well resolved in the AQCD. The findings of Carrothers and Evans (p.8-253, L1) tend to question this assumption. A statement should be made either that this is still an open question, or that the general assumption regarding the impact of measurement error on effect estimates still holds.

Section 8.4.8.4 (beginning p.8-264) largely describes the measures of PM exposure used in the several cohort studies. As opposed to the preceding section on measurement error in the time series studies, there is little attempt to interpret the role of measurement error in impacting estimates of effect in the cohort studies.

Thus, there remain a number of issues to be addressed in this important chapter and will need to be reviewed again.

Chapter 9 was found to be inadequate in only offering a recapitulation of specific details and not an integrative synthesis that brought together the information presented in the chapters in a way that provide a clear and concise description of what is know regarding particulate matter and adverse health and welfare effects. Rather than revising this chapter, *per se*, it was suggested to start over with an entirely different perspective based on a set of integrating questions that would serve to initiate the subsequent discussions. The NCEA staff was asked to formulate those questions into an outline for the chapter. A teleconference was scheduled for October 3 at which time the Panel would provide a consultation on proposed questions, which would then serve as the basis for rewriting Chapter 9. This teleconference was, in fact, held that day, and the Panel discussed and generally concurred on the restructured framework presented by the Agency.

There was a wide range of views on the Executive Summary from being moderately satisfied that it did integrate and summarize the large volume of complex information in the document to suggestions that it was too detailed and in some cases, too elementary. There are clearly significant inconsistencies in how the various topics are treated, and thus significant revision will be needed. However, the development of a truly integrative synthesis chapter should then provide a much better basis for extracting the key information from the AQCD and presenting it in the Executive Summary. Thus, the combination of the comments provided by the panel members and thinking afresh about the nature of the Executive Summary based on a new Chapter 9 should provide an appropriate path toward an appropriate summary for the document.

The CASAC PM Review Panel looks forward to seeing further improvements in this draft of the PM AQCD. The Panel wishes the Agency well in this important endeavor.

Sincerely,

/Signed/

Dr. Philip K. Hopke, Chair
Clean Air Scientific Advisory Committee

Appendix A – Review Comments from Individual CASAC Particulate Matter Review Panelists

Appendix B – Roster of the CASAC Particulate Matter Review Panel

Appendix A – Review Comments from Individual CASAC Particulate Matter Review Panelists

This appendix contains the preliminary and final written comments of individual members of the Clean Air Scientific Advisory Committee (CASAC) Particulate Matter (PM) Review Panel who submitted such comments electronically. The comments are included here to provide the all suggested edits, a full perspective, and range of individual views expressed by Subcommittee members during the review process. These comments do not represent the views of the CASAC PM Review Panel, the CASAC, the EPA Science Advisory Board, or the EPA itself. The consensus views of the CASAC PM Review Panel and the CASAC are contained in the text of the report to which this appendix is attached. Panelists providing comments are listed on the next page, and their individual comments follow.

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Dr. Frederick J. Miller

Draft Review Comments on 4th External Review Draft of the PM Criteria Document Fred J. Miller, Ph.D.

6. Dosimetry of Particulate Matter

General Comments

The dosimetry chapter for particulate matter has been greatly improved in the fourth external review draft compared to the third draft. The authors have added material on the comparison of dosimetry in laboratory animals versus humans that assists in the interpretation of toxicological effects and their potential relevance to effects in humans. In addition, detailed information has been added on regional and total respiratory tract deposition as a function of age for various particle sizes. However, the material that has been added on this topic is primarily a direct lifting of information from a RIVM report, and this report suffers from the writing bouncing around and results not being succinctly presented. For example, it would be better for the EPA authors to rewrite the material describing a particular region and examining deposition as a function of age before moving on to other regions or alternatively taking particles of a given size mode (ultrafine, fine, coarse) and then discussing deposition as a function of age for the various respiratory tract regions. As it is, the description is currently a potpourri of information and makes it difficult for the reader to extract the salient points.

Most of the technical errors present in the third external review draft have been corrected; however, the authors have failed to address some of the deficiencies pointed out by CASAC at the last review. In addition, the new material on interspecies dosimetry contains a number of significant technical errors that must be corrected, as noted below in the Specific Comments section. The summary section carries forward some of these errors, and it also contains errors in statements based on data that are only scantily presented via Figure 6-10 but that were presented in detail in the 1996 PM Criteria Document. This reviewer would be reluctant to assume that all technical errors will be corrected by the authors and that the dosimetry chapter can be brought to closure without another review by at least a subgroup of the PM Review Panel. The dosimetry chapter is intended to provide the necessary background for the interpretation of the deposition and fate of inhaled particulate matter in light of current knowledge. In its current form it fails to do this.

Specific Comments

- p. 6-17 The deposition studies in men and women by Kim and colleagues are described and repetitive statements are made that deposition is greater in women in the TB region and that total lung deposition of ultrafines was slightly greater in women than men. As requested before by this reviewer, where are the statistical tests of these differences that show support for the statements that are being made? Looking at Fig. 6-7, even if the trends are there and the differences can be

shown to be “statistically significant,” the differences are not likely to be biologically significant as they are on the order of only a few percentages in deposition fraction. The authors greatly exaggerate the differences in the description of the figure legend for Fig. 6-7 by talking about percent increases when describing a deposition fraction changing from 5.7 to 6.7 and stating this represents a 20% increase; certainly the potential for effects of determining a 1% difference in deposition fraction is highly unlikely. In short, a better balance is needed for the description of the results of these studies.

- p. 6-21, l. 21 The greater deposition in the left versus right lung in the study by Bennett et al. are stated to have a normalized ratio of 1.58 for 3.5 : m particles. By comparison, the MPPD model yields a L/R ratio of 1.02 using various lung geometries (Yeh and Schum 5-lobe symmetric, stochastic lungs with least and most number of TB airways). The difference between the MPPD model calculations and experimental measurements of Bennett can be attributed to the differences in inhalation regimen. Bennett's experiment included an inhalation of 40 ml bolus to a lung depth of 70 ml where most deposition is by impaction in the TB airways. The MPPD model calculates deposition of particles duration a breathing cycle with particles depositing in the TB region by impaction and PUL region by sedimentation.
- p. 6-23, l. 18 Replace “surface dose expressed a” with surface dose expressed as”.
- p. 6-26 In the description of the Kim et al. (2000) study, the statement is made that total lung deposition rate was found to be 34 times greater during moderate exercise than during rest for all particle sizes. The Criteria Document states that exercise may increase the health risk from particles because of increased large airway deposition and that women may be more susceptible to this exercise induced change. This raises the question as to a need for epi studies to examine whether gender differences in relationship to PM exposure and exercise do indeed result in different responses to particulate matter compared to men.
- p. 6-29, l. 8 In this paragraph describing the work of Musante and Martonen (1999), the statement is made that TB fractional deposition was found to be a monotonically decreasing function of age for all sizes and that total fractional lung deposition was generally higher in children than adults with children of all ages showing similar total deposition fractions. The monotonic relationship arises because of the way the authors scaled the anatomical data for the adult down to the lung size for children and does not necessarily reflect the reality of what one would obtain for deposition in children if the calculations were based upon actual lung geometries. This point is further discussed later on with the results from the CIIT/RIVM multipath deposition model for children.

- p. 6-30, l. 24 The statement here that children may still have deposition per unit surface area comparable to adults is in direct conflict with the statement made on lines 21 and 22 of the previous page. Which do the Criteria Document authors ascribe as the correct statement?
- p. 6-49, l. 1 While the statements in this paragraph based on theoretical calculations by Falk et al. (1997) are generally true, the higher flow rate results can be shown to depend upon the specific anatomical lung model used for the calculations. Using MPPD, the 5-lobe symmetric lung gives different results from the stochastic lung model. The stochastic lung model predicts significant deposition in the first 7 generations and only slight deposition in the pulmonary region; however, the 5-lobe symmetric model gives high deposition in the first 7 generations and even larger deposition in the alveolar region, a result that is more consistent with the predictions of Falk et al. (1997).
- p. 6-52 In the studies by Kreyling et al. (2002), results are presented in the Criteria Document for time points ranging up to one week with the showing of limited particle translocation into secondary organs. The longer term results are different for these studies and will be published shortly. While the Criteria Document authors would not necessarily be aware of this result, the sentence at the end of the paragraph (i.e., lines 1416) is not correct for longer term translocation of ultrafine iridium particles.
- p. 6-54 While not pointed out in the Criteria Document, the results of Takenaka et al. (2001) give a strong contrast to the results of Kreyling et al. (2002) and basically indicate that the results for ultrafine particles depend upon the type of particle. This point is not really made in the Criteria Document but should be because the results for real world solid ultrafine particles probably lie in between the extremes found by Takenaka for silver and Kreyling for iridium.
- p. 6-57, l. 7 Remove recent from the description of the study by Svartengren et al. since it was published in 1996 and clearly is no longer a recent study.
- p. 6-73, l. 16 Delete the sentence starting with “A variation of these models” as later on in the dosimetry chapter results for children are indeed presented.
- p. 6-83, l. 16 While the ICRP’s LUDEP model calculates deposition from 0.001 : m up to 100 : m, the calculations are unreliable for particles below 0.01 : m. This is because these very small particles behave more like gases and axial diffusion is not included in the calculations. Thus, presentation of results from LUDEP (and for that matter from the MPPD model) should be restricted to those for particles above 0.01 : m in physical size.

- p. 6-88, l. 2 The brochure for the MPPD states the CIIT Centers for Health Research and not the Chemical Industry Institute of Technology. In addition, the text should be modified to reflect the fact that the MPPD was developed by CIIT with partial funding from the Netherlands Ministry of Housing, Spatial Planning and the Environment.
- p. 6-88, l. 16 The text is unclear as to what “first principles” are being referred to in this sentence.
- p. 6-92 Many variables listed in Table 6-5 are reported to too many digits. FRC, URT volume, and TLC should be reported to the nearest integer. In the title of the table, the reference should be to the MPPD model and not to CIIT/RIVM.
- p. 6-92, l. 6 This sentence is factually incorrect unless “increase” on line 8 is replaced with “decrease”. With this change, the sentence follows from the results shown in Figure 6-17.
- p. 6-95 The data in Figure 6-18 is based on information reported in Winter-Sorkina and Cassee (2002) where version 1 of the MPPD model was used. While the MPPD software is publicly available, the children’s geometry files are in the process of being published as well as the computational approach used to solve for the dosimetry of particles. In fact, the most current version of MPPD contains two major changes: (1) Expressions to calculate head deposition have been modified. The old ones assumed Becquemin's data to correspond to the deposition fraction (inhalation + exhalation) while the data in the newest version of MPPD model designates deposition efficiency, and (2) Lung geometries have changed. (the default value for FRC, surface areas, alveolar volumes, and the number of alveoli) based upon additional improvements to the methodology. Thus, some of the relationships depicted in Figure 6-18 have changed. Given all of the other changes that need to be made in various figures in Chapter 6, EPA should obtain the latest version of MPPD before redoing the figure.
- p. 6-92, l. 12 The discussion of deposited mass rate in relationship to age can be misleading. For example, if one normalizes for the volume inhaled, then the TB deposition fraction is independent of age.
- p. 6-96, l. 10 The units on the alveolar surface area in adult lungs obtained by Gehr et al. (1978) are incorrect. They should be m². On line 12, the words “pulmonary 2” need to be replaced by “tracheobronchial” in order for the sentence to make sense. The statement beginning on line 12 about how many times greater are the tracheobronchial deposition fraction and mass rate per unit surface area for certain particle sizes is confusing as written. Even if these ratios are factually correct, the current text adds little to what could just as easily be stated as “due

to the large increase in surface area in the pulmonary compared to the tracheobronchial region, dose metrics typically have larger values for the TB region compared to the pulmonary region”.

- p. 6-96, l. 18 While the text here has been lifted verbatim from Winter-Sorkina and Cassee (2002), this sentence is lifted in its entirety from Mauderly (1979), who actually attributes the finding to the work of Thurlbeck (*Thorax* 22: 483, 1967).
- p. 6-97 In Table 6-6, “FRM” should be “FRC”.
- p. 6-97 In Fig. 6-19, the last column of panels is nothing more than a blowup of the last part of the panel in the same row just preceding it. This reviewer would suggest removing the last column of panels, thereby allowing the two remaining panels to be larger. The Y-axis for the first column of figures should be changed from “% Deposition” to “Deposition Fraction” to provide better agreement with other figures and textual descriptions contained in the rest of the chapter.
- p. 6-98, l. 16 Suggest adding “(see Panel a-2 of Figure 6-19)” after “1 : m”. Also, the next sentence should start a new paragraph.
- p. 6-99 Figure 6-20 results are incorrect. A back of the envelope calculation shows that the total : g deposited in an 8 hour period for rats exposed to 100 : g/m³ is no more than 2-3 : g. Given the rat lung weight of 4.34 g in Table 6-6, there is no way that a number like 90 : g per g lung is correct. The values for humans are also incorrect. This figure needs to be redone.
- p. 6-99, l. 3 Delete the abbreviation TH and spell out thoracic since the abbreviation is not used anywhere else. The statement about equivalent thoracic deposition in rats being obtainable with 0.5 to 0.75 of concentrations of humans is only correct if one restricts the comment to particles < 2.5 : m.
- p. 6-99, l. 6 This sentence discusses relative concentrations between rats and humans for comparable thoracic deposition between the species and makes the point that for coarse particles the deposition ratios are very sensitive to particle size. To avoid the potential for readers to misuse the species dose ratios that are presented in Figs. 6-19 and 6-20, it is suggested that the equation from Miller (*Inhal. Toxicol.* 12:12571259, 2000) be added.

To use these dose ratio plots, the following equation applies for exposure (E) levels in humans (H) and rats (R) that yield equivalent doses for a given dose metric when both species are exposed for the same length of time:

$$E_H = \frac{E_R}{X}$$

where X is the dose ratio for a specific particle size and given dose metric.

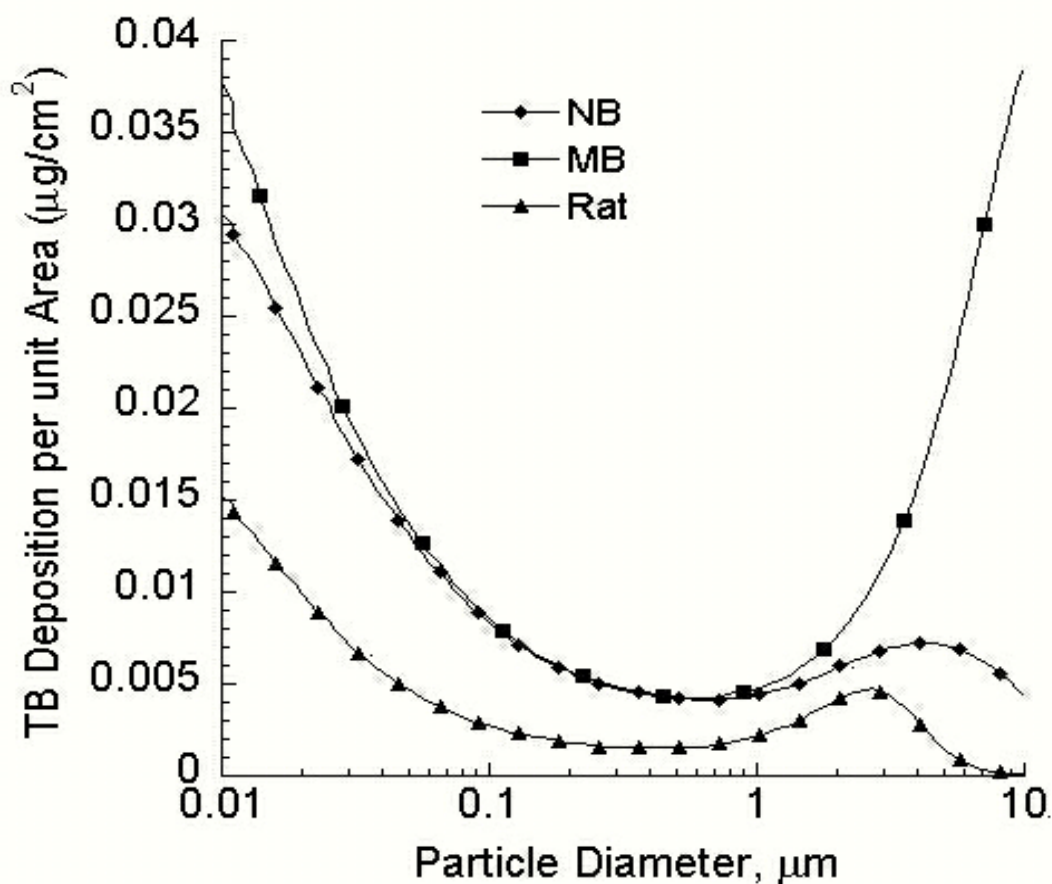
In addition, while Fig. 6-20 is technically correct, the normalization for thoracic region deposition to g of PM per g of lung is not particularly useful. Moreover, if the figure is retained, the point should be made that these dose ratios are only relevant for brief exposures because they do not take into account the clearance of particles. In fact this caveat, if present in the current chapter, was not apparent to this reviewer.

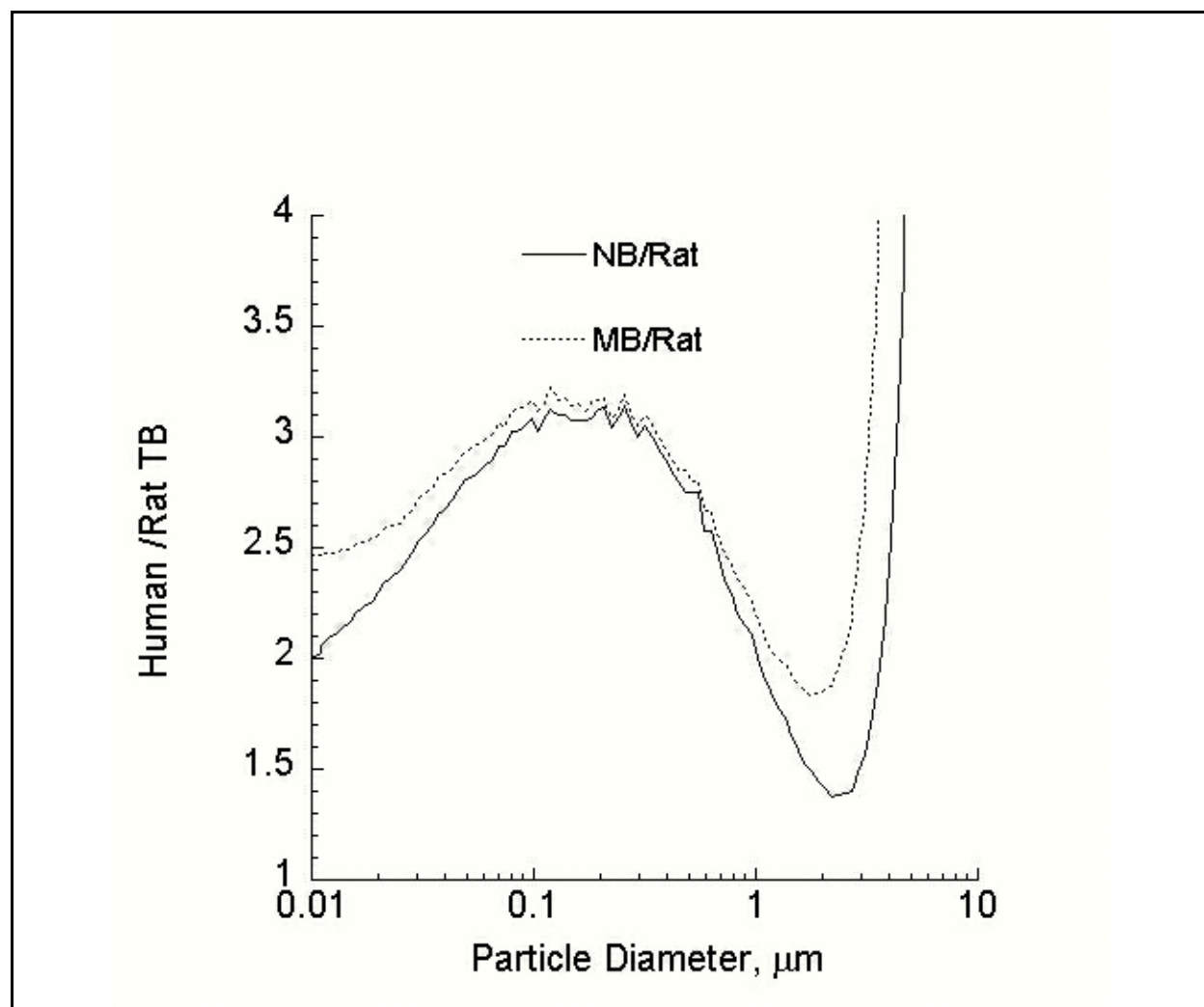
- p. 6-100 Table 6-7 gives regional respiratory tract surface areas for rats and humans. The line with data ascribed to CIIT/RIVM is not correct. The entries in this row all refer to various values published in the literature. Moreover, they are not used in the MPPD model developed by CIIT nor are they derivable from any data in that model. Footnote b makes the point that Winter-Sorinka and Cassee (2002) reported these data but they did not get the values from MPPD.
- p.6-100 Figure 6-21 presents data using EPA default values for surface area. The Y-axis denotes : g PM per cm² surface area for the TB and pulmonary regions but the figure legend states the units are : g PM per m². Probably the former is correct. However, even if the units are : g PM per cm² surface area, there is no way the numbers themselves are correct.
- p. 6-101 The units are incorrect for Figure 6-22, and the data values do not make sense for an eight hour exposure to 100 : g/m³. Using the MPPD model and the surface areas generated from that model, Panels a-1, a-2, b-1, and b-2 have been recalculated and the results are given in figures appearing at the end of my comments on this chapter.
- p. 6-101, l. 3 At the bottom of the page (i.e., line 3 below Figure 6-22) the statement is made that for coarse particles much higher exposures may be required for rats to obtain equivalent normalized doses. Given the poor inhalability of coarse mode particles by rats, a higher concentration really will not help much. Either a larger animal species (e.g., dog, monkey) needs to be used or else an endotracheal inhalation system for rats should be used. The point is that the current sentence implies you just have to up the concentration when in fact few inhaled coarse mode particles get to the thorax no matter what the concentration is.

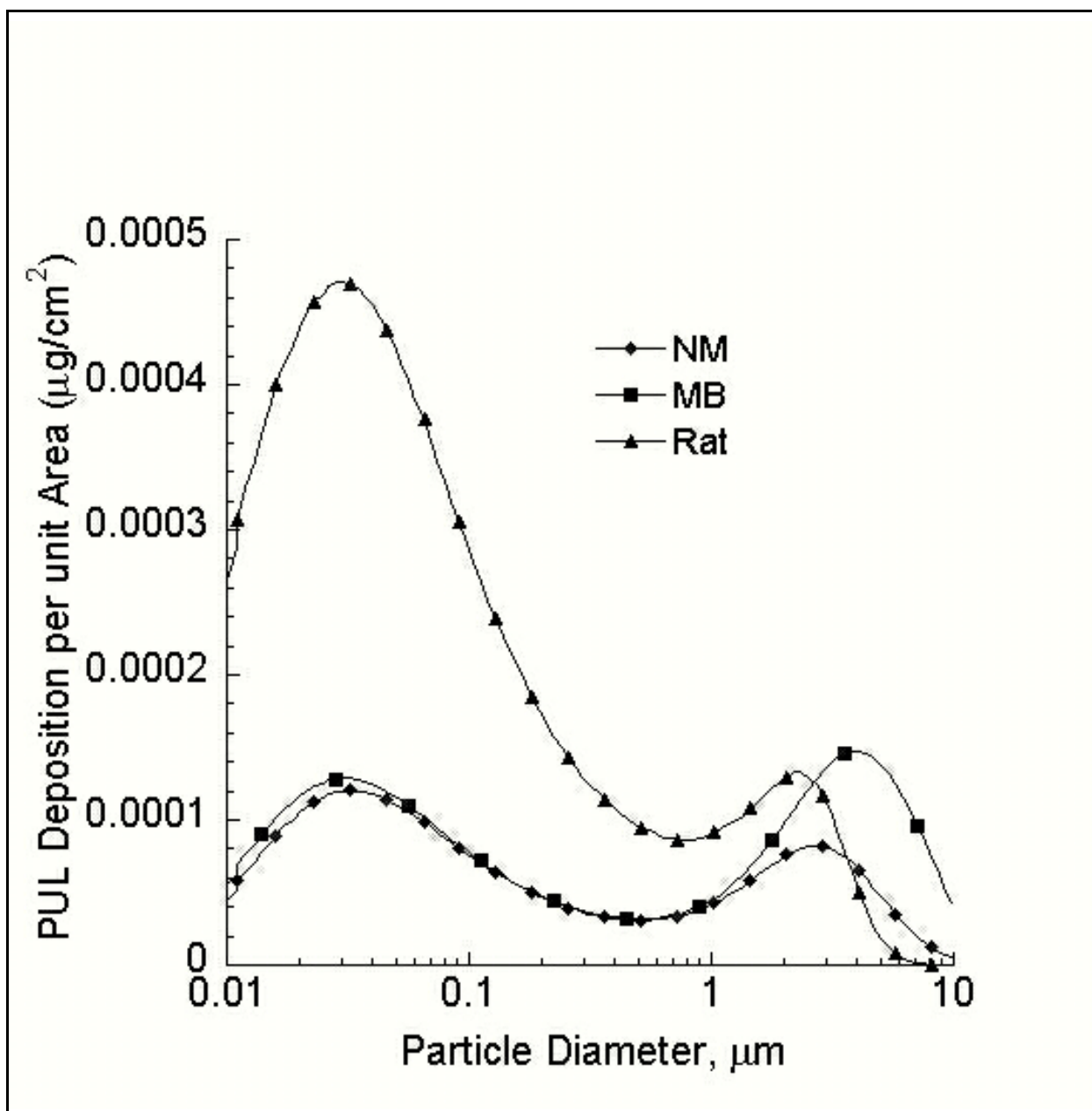
- p. 6-101, l. 2 (following Fig. 6-22) The statement is made that for fine particles, normalized human and rat deposition is comparable. This is an incorrect statement as this reviewer does not view dose ratios on the order of 2 to 2.5-fold as being “comparable.”
- p. 6-102 The Summary and Conclusion section, while improved over the previous version, is still weak. More factual information needs to be brought forward as compared to many of the generalizations that are currently there. The textual changes, incorrect statements, and technical errors noted about various topics earlier in my review comments need to be carried forward to the summary section. Specifically, the gender difference comments I made on p. 6-17 need to be addressed and then brought forward to the summary.
- p. 6-103, l. 2 The statement that total fractional lung deposition for 0.04 μ m and 0.06 μ m particles also appears to be greater in females than males is an overstatement unless statistical significance can be established for these differences in deposition fraction. In addition, the statement that for coarse mode particles the total fractional deposition increases in females is an overstatement since 1 μ m particles show negligible differences as well as for 3 μ m; only possibly for 5 μ m is there a real gender difference for deposition of this size particle.
- p. 6-103, l. 20 The experimental data by Becquemin et al. (1991) do not support the statement that ET and TB deposition is greater in children than adults. ET deposition is less in children while TB deposition is greater. This is also demonstrated by the modeling results presented in Figure 6-17.
- p. 6-105 The authors should state if the bullets on trends and peaks in deposition refer to humans, animals, or both species. Some specific bullet comments are:
 (1) The 3rd bullet makes the statement that particles in the accumulation mode (0.1 to 10 μ m Dp) size range have the lowest deposition fraction in all three regions. This statement is only correct for the ET and TB regions. Coarse mode particles have a lower deposition fraction in the alveolar region than do accumulation mode particles.
 (2) The 4th bullet says coarse and ultrafine particles have higher deposition fractions. Higher than what? The reader should not be expected to fill in “accumulation mode” plus the correction noted above about bullet 3. The peak in TB region deposition for coarse mode particles is incorrectly stated as between 5 and 10 μ m. Referring to the 1996 PM Criteria Document or to Figure 9 of Miller (Inhal. Toxicol. 12: 19-57, 2000), one sees that the peak is between 4-6 μ m for the TB region.
 (3) The 5th bullet should be deleted. As explained in my earlier comment (p. 6-83, l. 16), the LUDEP and MPPD models give unreliable deposition estimates for particles < 0.01 μ m in physical diameter since the code for these models does not include axial diffusion, which is an important transport mechanisms for

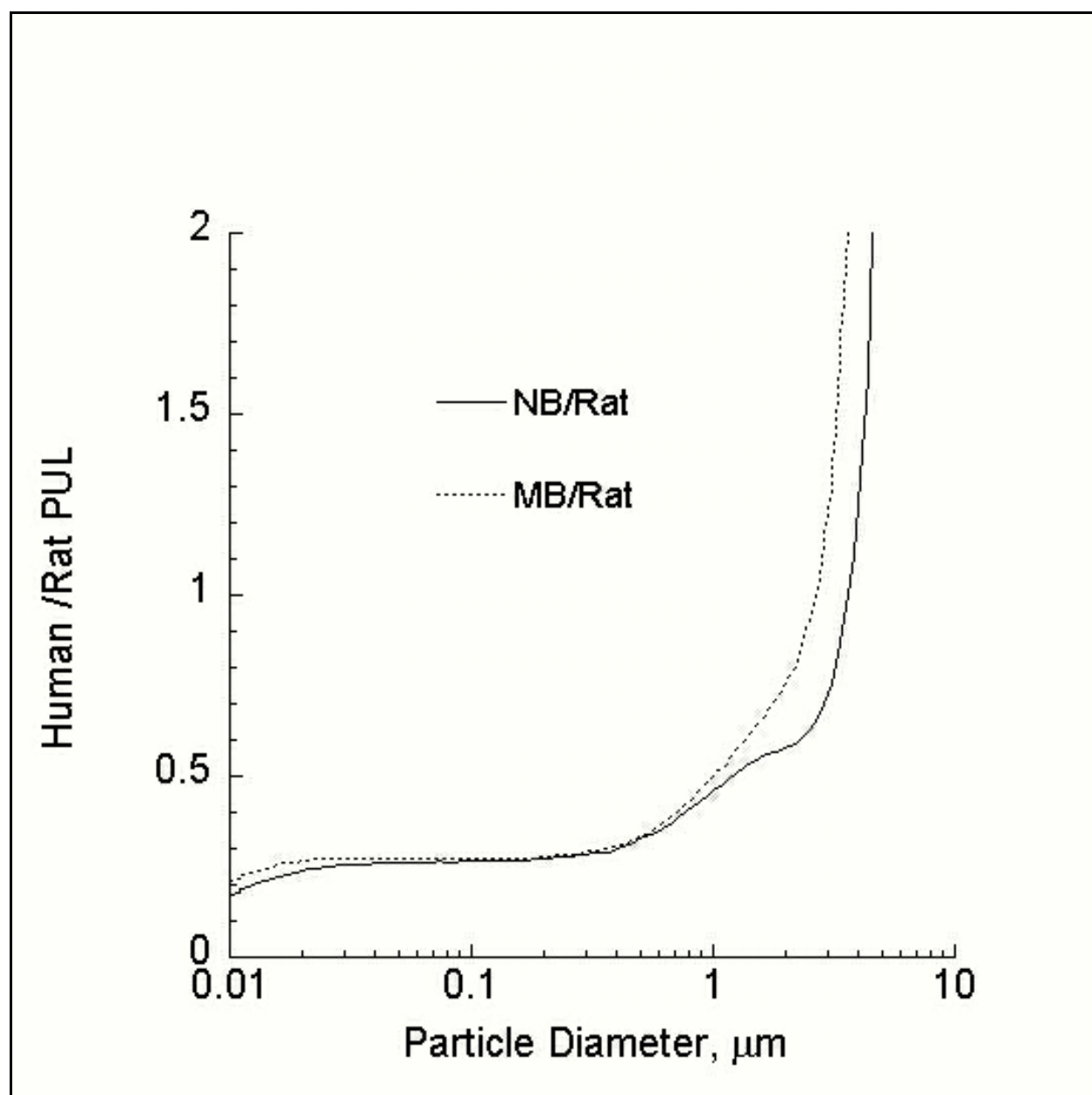
particles this small.

(4) The 8th bullet states that exercising subjects receive higher doses of particles per cm² of lung surface than subjects at rest. This statement is vague and is only partially correct depending upon what meaning the authors are conveying by the use of the word lung. Many persons use lung to refer to tracheobronchial and pulmonary regions combined (i.e., the thoracic region). The level of exercise is not stated and the statement clearly would not hold at heavy exercise given the switch to oronasal breathing when ventilatory drive exceeds about 35 L min⁻¹. Fine particle mass per unit area is likely to increase with exercise, but, for example, the mass per unit area in the TB region of 5 : m particles with light exercise is only about 90 % of what it is at rest. The authors need to make more accurate statements about exercise in relationship to dose metrics because exercise is indeed an important factor in dosimetry of PM.









7. Toxicology of Particulate Matter in Humans and Laboratory Animals.

General Comments

Often the authors of this chapter strain to make the case for biologic plausibility despite astronomically high doses of particles used in comparison to real world human exposures. Not as often do they state that caution is needed in interpreting the results for humans. This reviewer would urge a greater balance in the statements for support of the epidemiological results arising from some of the studies described in Chapter 7. That being said, the authors have done an excellent job in capturing the overall thrust of types of studies that have been conducted in animals. Some additional studies published prior to the end of 2002 should be added that give mechanistic insights (Reverdy et al., *Inhal. Toxicol.* 12: 283-289, 2000) or that compare species differences in response to the same particle (Bermudez et al., *Toxicol. Sci.* 70: 89-97, 2002; Hext et al. *Ann. Occup. Hyg.* 46: 191-196, 2002).

Specific Comments

- p. 7-33 The first paragraph makes the point that metals are at low concentrations in the ambient atmosphere and that metals found at concentrations less than 0.5 g/m³ were not reviewed in the previous Criteria Document. The authors then go on to state that more recently published data from high dose laboratory animal studies tend to indicate that particle associated metals are among likely potential candidates for inducing adverse effects attributed to ambient PM. The reader cannot tell from these sentences whether the point is the current draft will examine studies in metals that are found at low concentrations or that the studies that are presented based upon high dose exposures are still considered sufficient for implicating metals as contributing to adverse effects.
- p. 7-82, l. 15 This paragraph provides an excellent summary of the case for how there may be a neurogenic basis for particulate matter inflammation and should be included in the Summary section for the chapter to a greater extent than it currently is.
- p. 7-84, l. 20 In the discussion of the Lee et al. study, the point clearly comes across that instillation studies may be relevant to examining potential mechanisms but that these studies have to be approached with a degree of caution. Moreover, the authors should make it clear that, relative to risk assessment, inhalation studies should be the basis for using results from animal studies in extrapolating to humans.
- p. 7-87, l. 26 The sentence discussing rodent models of disease and stating criteria for judging the appropriateness of these models is not very useful in its current form. The authors should provide some examples of the issues.

- p. 7-94, l. 22 The description of the Kleeberger study discusses an overall magnitude of change being small and not being correlated with changes in macrophage phagocytosis. The dose used in this study of 10 mg/m³ carbon with 285 g/m³ of sulfate for a 4-h exposure of mice is a tremendous dose. The primary usefulness of this study has to do with the genes that were identified as potentially controlling susceptibility.
- p. 7-99, l. 17 The lead in sentence to this paragraph represents an overstatement of the results from the Diaz-Sanchez et al. study relative to extending the results for ambient combustion diesel particles containing particulate matter and their potential for significant effects on allergic asthma. The Diaz-Sanchez et al. study used 115 g of diesel particles in each nostril of the nose of subjects. To deliver any kind of comparable levels from ambient particles would require astronomical exposures. Thus this paragraph while indicating the potential is stating the potential in a much stronger context than is warranted by the data.
- p. 126, l. 1 The description of the Nemmar et al. (2001) study using albumin nanocolloid particles instilled in hamsters provides some puzzling results. There is a temporal response at the 5, 15, and 30 minute sampling times, but the response at 60 minutes goes counter to this trend in a drastic manner. So the question arises, what is happening at 60 minutes? The results would indicate a time scale response of only a matter of minutes. What is the evidence for this from other studies? If none are available, then the study should be so noted as potentially representing a deviation of the likely time response pattern from particulate exposure.

9. Integrative Synthesis

General Comments

Overall, the authors have done an excellent job in this chapter of capturing the salient points and providing an integration of the results from multiple areas of research. The description of the legislative requirements and the sequence of events that EPA has entertained relative to particulate matter standards is useful and provides an excellent introduction to the chapter. The section on describing the organization of the chapter is also good because it sets the reader up for what is to follow. There are a number of areas for which the wording needs to be improved to provide clarity or for which there are technical errors in interpretation; these aspects are noted in the Specific Comments section below.

The Integrative Synthesis chapter does a good job of describing the types of endpoints that appear to be affected by PM exposure. However, there is currently no attempt to identify where the strongest case can be made for the need for PM standards in light of the various studies that have been conducted and no specific attempt to identify the appropriate indicator variable be that PM 10, PM 2.5, or PM 10-2.5. I believe that the addition of such a subsection to Section 9.9

would be most informative. In that regard, a quick tabulation of the studies reported in tables in Chapter 9 is given below for some of the endpoints. One quickly sees that PM 10 provides the most consistent indicator of various types of effects ranging from mortality to respiratory morbidity. PM 2.5 also does a reasonably good job for mortality and respiratory morbidity but is much poorer as an indicator variable for cardiovascular morbidity as is PM 10. In fact, for cardiovascular morbidity, PM 10-2.5 does almost as good a job as does PM 10. While I recognize that the table is a relatively simple one and does not account for various investigators analyzing the same city by different methods or over a different period of time, the point is that the data in Chapter 8 provide a wealth of information for attempting to identify the appropriate PM indicator variable and the level of that variable against which public health should be protected.

Endpoint	Total No. Analyses	PM 10		PM 2.5		PM 10-2.5	
		No.	% Positive	No.	% Positive	No.	% Positive
Mortality	39	26	62	29	59	19	12
Cardiovascular Morbidity	18	18	56	8	38	6	50
Respiratory Morbidity	24	23	78	13	62	7	29

Specific Comments

- p. 9-11, l. 24 The acknowledgment is made that PM 2.5 includes some particles between 1 and 2.5 m Da from the lower tail of the coarse mode. The question arises as to the legal implications of this overlap relative to reaffirming or revising the current 2.5 standard and the possible introduction of a PM 10-2.5 standard.
- p. 9-11, l. 30 Text is provided that notes that size fractions are usually specified by a 50% cut point size. Specifically stated are the collection of 50% of 2.5 m particles and a rejection of 50% of these particles. Yet these particles are 100% inhalable in humans. Thus conception ally the mass deposited in the human lung would be about twice what you would get if you used PM 2.5 monitoring samples. The question arises as to what change is needed in the concentration to capture the actual mass deposited in humans that represents the discrepancy between the penetration and inhalability curves if one is comparing equivalent exposure scenarios between animals and humans (i.e., extrapolating animal results directly is not straightforward for exposure concentration since inhalability and the sampler penetration curves must be taken into account.)
- p. 9-13 Fig. 9-5 provides a size cut curve for inhalable particulate matter that is labeled IPM. This curve does not match the experimental data of Breyse and Swift (*Aerosol Sci. Technol.* 13:459464, 1990). The curve has been generated from

definitions given by the American Conference of Governmental Industrial Hygienists (1994). However, the experimental data should carry more weight and a fitted curve as available from Ménache et al. (*Ann. occup. Hyg.* 39:317328, 1995) should be at a minimum added to the figure or at best added and the IPM curve deleted.

- p. 9-20 Fig. 9-7 presents an interesting cartoon illustrating the particle bound water that should be removed as well as that which should be retained. Are there data from experimental studies that can assess the accuracy of the descriptive presentation? The appropriate removal of particle bound water is a topic that could influence whether or not cities are in compliance for various aspects of any PM 2.5 standard. Thus, this topic should be further discussed in the Integrative Synthesis chapter and to the extent that data are currently available, the text should be expanded. If data are not available to provide a range of uncertainty around the amount of water that is to be removed from the sample, this is an important research need that should be identified as part of the PM Criteria Document review process.
- p. 9-26, l. 4 The discussion here illustrates the amount of variability that can be present in annual mean concentrations. Typically annual mean concentrations are within 5 g/m³ of each other in urban areas but the spread in values can be much greater if consolidated MSAs (CMSAs) are considered. The statement that even with some MSAs those concentrations measured at separate sites on individual days can differ by over 100 g/m³ raises an important question relative to monitoring for compliance. Specifically, what does this description of variability say for limited sites being used to define compliance in any given city?
- p. 9-27 Fig. 9-9 shows concentration differences in three cities. It is interesting to note that 79% of the sites in Chicago, Illinois vary by less than 5 g/m³ so that one could contend that spatial variability is not an issue in Chicago. However, two-thirds of the concentration differences exceed 5 g/m³ for Detroit, Michigan. With these two cities as examples, the conclusion would be that the current standard of 15 g/m³ annual for PM 2.5 is potentially greatly affected by spatial variability in a city. This implies that an extensive monitoring network for compliance needs to be developed in order to accurately capture the annual exposure for some metropolitan areas.
- p. 9-30 The regression shown for daytime total personal exposure to PM 10 versus ambient PM 10 concentrations using data from the PTEAM study shows a very poor correlation coefficient (only about 14% of the variability in the data is explained). If this is typical, there is a potential difficulty in trying to use these kinds of curves for determining total personal exposure; looking at the variability of this parameter becomes important as it would have potential for identifying the extent of the population that might be affected by exposures to

specified levels of particulate matter.

- p. 9-38, l. 20 The statement is made that there is still no published information that would suggest differences in exposure relationships for healthy versus sensitive populations. While these data may not be published, it seems intuitively obvious that those individuals with disease such as COPD have different activity patterns than normal healthy subjects.
- p. 9-40, l. 18 The authors need to be consistent in statements about sedimentation. In Chapter 6 (p. 6-6) sedimentation is described as important for particles greater than 1 m in aerodynamic diameter. However, in Chapter 9, the statement is that particles with an aerodynamic diameter greater than 0.5 m mostly are affected by sedimentation out of the air stream. There is a need to be consistent and to this reviewer, the Chapter 6 statement is the accurate one.
- p. 9-41, l. 18 Similarly to discrepancies on sedimentation, the authors refer to the coarse mode size range as being that containing particles greater than 1 m in size. However, in many other places in the Criteria Document the coarse mode is defined as particles greater than 2.5 m in size. This again points to the need for the Criteria Document to use a consistent definition of the different size range modes.
- p. 9-43, l. 11 The comments of this reviewer made about gender differences in Chapter 6 should be looked at and the changes brought forward to Chapter 9. Specifically, the comments made about the text on page 6-17.
- p. 9-43, l. 14 A number of statements are made about children showing particular effects in terms of particle exposure. The statement about greater total respiratory tract deposition in adults (possibly as much as 50% greater for those less than 14 years old than for adults greater than 14 years) is made and appears to be based on the studies of Bennett described in Chapter 6, p. 30. However, that result only applied to the 4.5 m particles. It does not hold for all particle sizes. For example, the 2 m experiments of Bennett showed no age dependency and no difference in total deposition between children and adults. A better description of the experimental data for children versus adults is needed in Chapter 9.
- p. 9-45, l. 3 The reference to CIIT as the Chemical Industry Institute of Technology is not correct. As the brochure for the MPPD model clearly indicates, the program was developed by the CIIT Centers for Health Research. In addition, the text should be modified to reflect the fact that the MPPD was developed by CIIT with partial funding from the Netherlands Ministry of Housing, Spatial Planning and the Environment.
- p. 9-46, l. 23 The statement that the clearance of particles from the alveolar region by

alveolar macrophages and their mucociliary transport is usually rapid and is less than 24 hours is factually incorrect. The 24 hour clearance refers to the tracheobronchially deposited particles while the clearance for alveolar deposition ranges on the order of weeks to months or years. Even for a fast phase component of alveolar clearance, it would exceed 24 hours.

- p. 9-49, l. 24 The authors indicate the need for dosimetric calculations to accompany instillation studies to provide better information for human risk assessment. While this is certainly the case, it should be restated here that risk assessments should primarily be based upon results from inhalation studies given the problems discussed in Chapter 6 that are present in conducting and interpreting instillation studies.
- p. 9-69, l. 1 This statement is biased. To make the statement, one would have to assume that effects are present but there is no power to detect them. However, it is also possible that it could represent a true no-effect situation. The sentence needs to be modified to reflect the duality of potential interpretations.
- p. 9-69, l. 18 Remove ozone from the list of water soluble toxic gases as ozone is clearly poorly soluble in water.
- p. 9-76, l. 10 The statement is made that Table 9-8 focuses on various PM indicators and excess risk as derived from single pollutant PM models. It would be useful to indicate in this paragraph why single pollutant PM model results were chosen to be presented as the basis for the table given that many of the authors also fit multi pollutant models.
- p. 9-91 Table 9-10 represents an important table describing cardiovascular and respiratory related morbidity effects size estimates. It may be useful to use this table to develop another table that would provide the indicator level and then the effect type with the proportion of studies being significant out of the total number described.
- p. 9-136 What does the * mean in Table 9-13?
- p. 9-137 Figure 9-23 does not relate to nor have implications for dose unless one assumes the same deposition fraction for children and adults. And we know based upon results presented in Chapter 6 that this is not the case. There is limited value in retaining this figure.
- p. 9-139 Section 9.10 has no references provided in the text in contrast to other sections in Chapter 9. In addition, the material that is included is speculative and includes only a general description of potential changes. This makes the section of limited value. What specific environmental effects that can be ascribed to PM

should form the basis of the section. Currently, the section is of limited value.

Final Review Comments on 4th External Review Draft of the PM Criteria Document

6. Dosimetry of Particulate Matter

General Comments

The dosimetry chapter for particulate matter has been greatly improved in the fourth external review draft compared to the third draft. The authors have added material on the comparison of dosimetry in laboratory animals versus humans that assists in the interpretation of toxicological effects and their potential relevance to effects in humans. In addition, detailed information has been added on regional and total respiratory tract deposition as a function of age for various particle sizes. However, the material that has been added on this topic is primarily a direct lifting of information from a RIVM report, and this report suffers from the writing bouncing around and results not being succinctly presented. For example, it would be better for the EPA authors to rewrite the material describing a particular region and examining deposition as a function of age before moving on to other regions or alternatively taking particles of a given size mode (ultrafine, fine, coarse) and then discussing deposition as a function of age for the various respiratory tract regions. As it is, the description is currently a potpourri of information and makes it difficult for the reader to extract the salient points.

One significant lack of responsiveness in the 4th External Review Draft concerns the request by CASAC to present dosimetry calculations for various real world exposure scenarios (both short term where deposition may be the driver and long term where retention after some particle clearance may be the driver) encountered by humans. This information is needed to put into perspective the dosimetry of PM for the various animal toxicology studies contained in Chapter 7 as to their relevance for establishing biological plausibility within some reasonable margin of exposure compared to human exposures. Failure to provide this requested information weakens efforts to identify or predict dose-response relationships in the animal studies and thereby extend any biological plausibility arguments made by the Agency in support of the effects seen in epi studies and for which EPA is making the case that they relate to PM indicators.

Most of the technical errors present in the third external review draft have been corrected; however, the authors have failed to address some of the deficiencies pointed out by CASAC at the last review. In addition, the new material on interspecies dosimetry contains a number of significant technical errors that must be corrected, as noted below in the Specific Comments section. The summary section carries forward some of these errors, and it also contains errors in statements based on data that are only scantily presented via Figure 6-10 but that were presented in detail in the 1996 PM Criteria Document. This reviewer would be reluctant to assume that all technical errors will be corrected by the authors and that the dosimetry chapter can be brought to closure without another review by at least a subgroup of the PM Review Panel. The dosimetry chapter is intended to provide the necessary background for the interpretation of the deposition and fate of inhaled particulate matter in light of current knowledge. In its current form it fails to

do this.

Specific Comments

- p. 6-17 The deposition studies in men and women by Kim and colleagues are described and repetitive statements are made that deposition is greater in women in the TB region and that total lung deposition of ultrafines was slightly greater in women than men. As requested before by this reviewer, where are the statistical tests of these differences that show support for the statements that are being made? Looking at Fig. 6-7, even if the trends are there and the differences can be shown to be “statistically significant,” the differences are not likely to be biologically significant as they are on the order of only a few percentages in deposition fraction. The authors greatly exaggerate the differences in the description of the figure legend for Fig. 6-7 by talking about percent increases when describing a deposition fraction changing from 5.7 to 6.7 and stating this represents a 20% increase; certainly the potential for effects of determining a 1% difference in deposition fraction is highly unlikely. In short, a better balance is needed for the description of the results of these studies.
- p. 6-21, l. 21 The greater deposition in the left versus right lung in the study by Bennett et al. are stated to have a normalized ratio of 1.58 for 3.5 : m particles. By comparison, the MPPD model yields a L/R ratio of 1.02 using various lung geometries (Yeh and Schum 5-lobe symmetric, stochastic lungs with least and most number of TB airways). The difference between the MPPD model calculations and experimental measurements of Bennett can be attributed to the differences in inhalation regimen. Bennett's experiment included an inhalation of 40 ml bolus to a lung depth of 70 ml where most deposition is by impaction in the TB airways. The MPPD model calculates deposition of particles duration a breathing cycle with particles depositing in the TB region by impaction and PUL region by sedimentation.
- p. 6-23, l. 18 Replace “surface dose expressed a” with surface dose expressed as”.
- p. 6-26 In the description of the Kim et al. (2000) study, the statement is made that total lung deposition rate was found to be 34 times greater during moderate exercise than during rest for all particle sizes. The Criteria Document states that exercise may increase the health risk from particles because of increased large airway deposition and that women may be more susceptible to this exercise induced change. This raises the question as to a need for epi studies to examine whether gender differences in relationship to PM exposure and exercise do indeed result in different responses to particulate matter compared to men.
- p. 6-29, l. 8 In this paragraph describing the work of Musante and Martonen (1999), the statement is made that TB fractional deposition was found to be a

monotonically decreasing function of age for all sizes and that total fractional lung deposition was generally higher in children than adults with children of all ages showing similar total deposition fractions. It should be noted in this paragraph that the monotonic relationship arises because of the way the authors scaled the anatomical data for the adult down to the lung size for children and does not necessarily reflect the reality of what one would obtain for deposition in children if the calculations were based upon actual lung geometries. This point is particularly important to make given that the MPPD results for children are being dropped from the chapter since the methodology for the lung geometries is awaiting publication but for which the lack of linearity is apparent in output from the model. Bottom line is that the point should be retained that children may have greater deposition of mass per unit area than adults but that this relationship may not be linear with age.

- p. 6-30, l. 24 The statement here that children may still have deposition per unit surface area comparable to adults is in direct conflict with the statement made on lines 21 and 22 of the previous page. The statement on the previous page is the correct one in the view of this reviewer. The authors need to be consistent on this point.
- p. 6-49, l. 1 While the statements in this paragraph based on theoretical calculations by Falk et al. (1997) are generally true, the higher flow rate results can be shown to depend upon the specific anatomical lung model used for the calculations. Using MPPD, the 5-lobe symmetric lung gives different results from the stochastic lung model. The stochastic lung model predicts significant deposition in the first 7 generations and only slight deposition in the pulmonary region; however, the 5-lobe symmetric model gives high deposition in the first 7 generations and even larger deposition in the alveolar region, a result that is more consistent with the predictions of Falk et al. (1997).
- p. 6-52 In the studies by Kreyling et al. (2002), results are presented in the Criteria Document for time points ranging up to one week with the showing of limited particle translocation into secondary organs. The longer term results are different for these studies and will be published shortly. While the Criteria Document authors would not necessarily be aware of this result, the sentence at the end of the paragraph (i.e., lines 1416) should probably have added a qualifier to indicate this applies to short-term exposures to ultrafine iridium particles.
- p. 6-54 While not pointed out in the Criteria Document, the results of Takenaka et al. (2001) give a strong contrast to the results of Kreyling et al. (2002) and basically indicate that the results for ultrafine particles depend upon the type of particle. This point is not really made in the Criteria Document but should be because the results for real world solid ultrafine particles probably lie in between the extremes found by Takenaka for silver and Kreyling for iridium.

- p. 6-57, l. 7 Remove recent from the description of the study by Svartengren et al. since it was published in 1996 and clearly is no longer a recent study.
- p. 6-83, l. 16 While the ICRP's LUDEP model calculates deposition from 0.001 : m up to 100 : m, the calculations are unreliable for particles below 0.01 : m. This is because these very small particles behave more like gases, and axial diffusion is not included in the calculations. Thus, presentation of results from LUDEP (and for that matter from the MPPD model) should be restricted to those for particles above 0.01 : m in physical size. In fact, the developers of the MPPD model recognize this limitation and do not provide an option for calculating deposition for particles < 0.01 : m in diameter.
- p. 6-88, l. 2 The brochure for the MPPD states the CIIT Centers for Health Research and not the Chemical Industry Institute of Technology. In addition, the text should be modified to reflect the fact that the MPPD was developed by CIIT with partial funding from the Netherlands Ministry of Housing, Spatial Planning and the Environment.
- p. 6-88, l. 16 The text is unclear as to what "first principles" are being referred to in this sentence.
- p. 6-92 Many variables listed in Table 6-5 are reported to too many digits. FRC, URT volume, and TLC should be reported to the nearest integer. In the title of the table, the reference should be to the MPPD model and not to CIIT/RIVM. This will no longer be an issue since the table can be deleted given that children's deposition results from MPPD are not being presented.
- p. 6-92, l. 6 This sentence is factually incorrect unless "increase" on line 8 is replaced with "decrease". With this change, the sentence follows from the results shown in Figure 6-17.
- p. 6-95 The data in Figure 6-18 is based on information reported in Winter-Sorkina and Cassee (2002) where version 1 of the MPPD model was used. While the MPPD software is publicly available, the children's geometry files are in the process of being published as well as the computational approach used to solve for the dosimetry of particles. In fact, the most current version of MPPD contains two major changes: (1) Expressions to calculate head deposition have been modified. The old ones assumed Becquemin's data to correspond to the deposition fraction (inhalation + exhalation) while the data in the newest version of MPPD model designates deposition efficiency, and (2) Lung geometries have changed. (the default value for FRC, surface areas, alveolar volumes, and the number of alveoli) based upon additional improvements to the methodology. Thus, some of the relationships depicted in Figure 6-18 have changed. Given all of the other changes that need to be made in various figures

in Chapter 6, EPA should obtain the latest version of MPPD before redoing the figure. However, the CASAC recommended not including the calculations for children so this becomes a non issue.

- p. 6-92, l. 12 The discussion of deposited mass rate in relationship to age can be misleading. For example, if one normalizes for the volume inhaled, then the TB deposition fraction is independent of age. Some caveat to reflect this should be added.
- p. 6-96, l. 10 The units on the alveolar surface area in adult lungs obtained by Gehr et al. (1978) are incorrect. They should be m². On line 12, the words “pulmonary 2” need to be replaced by “tracheobronchial” in order for the sentence to make sense. The statement beginning on line 12 about how many times greater are the tracheobronchial deposition fraction and mass rate per unit surface area for certain particle sizes are confusing as written. Even if these ratios are factually correct, the current text adds little to what could just as easily be stated as “due to the large increase in surface area in the pulmonary compared to the tracheobronchial region, dose metrics typically have larger values for the TB region compared to the pulmonary region”.
- p. 6-96, l. 18 While the text here has been lifted verbatim from Winter-Sorkina and Cassee (2002), this sentence is lifted in its entirety from Mauderly (1979), who actually attributes the finding to the work of Thurlbeck (*Thorax* 22: 483, 1967).
- p. 6-97 In Table 6-6, “FRM” should be “FRC”.
- p. 6-97 In Fig. 6-19, the last column of panels is nothing more than a blowup of the last part of the panel in the same row just preceding it. This reviewer would suggest removing the last column of panels, thereby allowing the two remaining panels to be larger. The Y-axis for the first column of figures should be changed from “% Deposition” to “Deposition Fraction” to provide better agreement with other figures and textual descriptions contained in the rest of the chapter. In addition, the X-axis should first start at 0.01 : m in the panels of the figure.
- p. 6-98, l. 16 Suggest adding “(see Panel a-2 of Figure 6-19)” after “1 : m”. Also, the next sentence should start a new paragraph.
- p. 6-99 Figure 6-20 results are incorrect. A back of the envelope calculation shows that the total : g deposited in an 8 hour period for rats exposed to 100 : g/m³ is no more than 2-3 : g. Given the rat lung weight of 4.34 g in Table 6-6, there is no way that a number like 90 : g per g lung is correct. The values for humans are also incorrect. This figure needs to be redone.
- p. 6-99, l. 3 Suggest deleting the abbreviation TH and spelling out thoracic since the abbreviation is not used anywhere else. The statement about equivalent thoracic

deposition in rats being obtainable with 0.5 to 0.75 of concentrations of humans is only correct if one restricts the comment to particles < 2.5 : m.

- p. 6-99, l. 6 This sentence discusses relative concentrations between rats and humans for comparable thoracic deposition between the species and makes the point that for coarse particles the deposition ratios are very sensitive to particle size. To avoid the potential for readers to misuse the species dose ratios that are presented in Figs. 6-19 and 6-20, it is suggested that the equation from Miller (*Inhal. Toxicol.* 12:12571259, 2000) be added.

To use these dose ratio plots, the following equation applies for exposure (E) levels in humans (H) and rats (R) that yield equivalent doses for a given dose metric when both species are exposed for the same length of time:

$$E_H = \frac{E_R}{X}$$

where X is the dose ratio for a specific particle size and given dose metric.

In addition, while Fig. 6-20 is technically correct, the normalization for thoracic region deposition to g of PM per g of lung is not particularly useful. Moreover, if the figure is retained, the point should be made that these dose ratios are only relevant for brief exposures because they do not take into account the clearance of particles. In fact this caveat, if present in the current chapter, was not apparent to this reviewer.

- p. 6-100 Table 6-7 gives regional respiratory tract surface areas for rats and humans. The line with data ascribed to CIIT/RIVM is not correct. The entries in this row all refer to various values published in the literature. Moreover, they are not used in the MPPD model developed by CIIT nor are they derivable from any data in that model. Footnote b makes the point that Winter-Sorinka and Cassee (2002) reported these data but they did not get the values from MPPD.
- p.6-100 Figure 6-21 presents data using EPA default values for surface area. The Y-axis denotes : g PM per cm² surface area for the TB and pulmonary regions but the figure legend states the units are : g PM per m². Probably the former is correct. However, even if the units are : g PM per cm² surface area, there is no way the numbers themselves are correct.
- p. 6-101 The units are incorrect for Figure 6-22, and the data values do not make sense for an eight hour exposure to 100 : g/m³. Using the MPPD model and the surface areas generated from that model, Panels a-1, a-2, b-1, and b-2 have been recalculated and the results are given in figures appearing at the end of my

comments on this chapter for particles $> 0.01 : m$ in diameter.

- p. 6-101, l. 3 At the bottom of the page (i.e., line 3 below Figure 6-22) the statement is made that for coarse particles much higher exposures may be required for rats to obtain equivalent normalized doses. Given the poor inhalability of coarse mode particles by rats, a higher concentration really will not help much. Either a larger animal species (e.g., dog, monkey) needs to be used or else an endotracheal inhalation system for rats should be used. While the current sentence implies you just have to up the concentration, the fact is that the lack of inhalability of particles larger than about $5 : m$ in rats means that few inhaled coarse mode particles get to the thorax no matter what the concentration is of these larger particles. This paragraph should be reworded to reflect this.
- p. 6-101, l. 2 (following Fig. 6-22) The statement is made that for fine particles, normalized human and rat deposition is comparable. This is an incorrect statement as this reviewer does not view dose ratios on the order of 2 to 2.5-fold as being “comparable.”
- p. 6-102 The Summary and Conclusion section, while improved over the previous version, is still weak. More factual information needs to be brought forward as compared to many of the generalizations that are currently there. The textual changes, incorrect statements, and technical errors noted about various topics earlier in my review comments need to be carried forward to the summary section. Specifically, the gender difference comments I made on p. 6-17 need to be addressed and then brought forward to the summary.
- p. 6-103, l. 2 The statement that total fractional lung deposition for $0.04 m$ and $0.06 m$ particles also appears to be greater in females than males is an overstatement unless statistical significance can be established for these differences in deposition fraction. In addition, the statement that for coarse mode particles the total fractional deposition increases in females is an overstatement since $1 m$ particles show negligible differences as well as do $3 m$ particles; only possibly for 5 is there a real gender difference for deposition of this size particle.
- p. 6-103, l. 20 The experimental data by Becquemin et al. (1991) do not support the statement that ET and TB deposition is greater in children than adults. ET deposition is less in children while TB deposition is greater. This is also demonstrated by the modeling results presented in Figure 6-17.
- p. 6-105 The authors should state if the bullets on trends and peaks in deposition refer to humans, animals, or both species. Some specific bullet comments are:
- (1) The 3rd bullet makes the statement that particles in the accumulation mode (0.1 to $1 : m$ D_p) size range have the lowest deposition fraction in all three

regions. This statement is only correct for the ET and TB regions. Coarse mode particles have a lower deposition fraction in the alveolar region than do accumulation mode particles.

(2) The 4th bullet says coarse and ultrafine particles have higher deposition fractions. Higher than what? The reader should not be expected to fill in “accumulation mode” plus the correction noted above about bullet 3. The peak in TB region deposition for coarse mode particles is incorrectly stated as between 5 and 10 : m. Referring to the 1996 PM Criteria Document or to Figure 9 of Miller (Inhal. Toxicol. 12: 19-57, 2000), one sees that the peak is between 4-6 : m for the TB region.

(3) The 5th bullet should be deleted. As explained in my earlier comment (p. 6-83, l. 16), the LUDEP model gives unreliable deposition estimates for particles < 0.01 : m in physical diameter since the code for this model does not include axial diffusion, which is an important transport mechanisms for particles this small. The MPPD model does not even treat particles this small.

(4) The 8th bullet states that exercising subjects receive higher doses of particles per cm² of lung surface than subjects at rest. This statement is vague and is only partially correct depending upon what meaning the authors are conveying by the use of the word lung. Many persons use lung to refer to tracheobronchial and pulmonary regions combined (i.e., the thoracic region). The level of exercise is not stated and the statement clearly would not hold at heavy exercise given the switch to oronasal breathing when ventilatory drive exceeds about 35 L min⁻¹. Fine particle mass per unit area is likely to increase with exercise, but, for example, the mass per unit area in the TB region of 5 : m particles with light exercise is only about 90 % of what it is at rest. The authors need to make more accurate statements about exercise in relationship to dose metrics because exercise is indeed an important factor in dosimetry of PM.

7. Toxicology of Particulate Matter in Humans and Laboratory Animals.

General Comments

Often the authors of this chapter strain to make the case for biologic plausibility despite astronomically high doses of particles used in comparison to real world human exposures. Not as often do they state that caution is needed in interpreting the results for humans. This reviewer urges the authors to achieve a better balance in the statements for support of the epidemiological results arising from some of the studies described in Chapter 7. That being said, the authors have done a good job in capturing in the various sections the overall thrust of the types of studies that have been conducted in animals. However, the summary section fails to provide a good summary of the important knowledge gained from the studies discussed earlier in the chapter. Some additional studies published prior to the end of 2002 should be added that give mechanistic

insights (e.g., Reverdy et al., *Inhal. Toxicol.* 12: 283-289, 2000) or that compare species differences in response to the same particle (e.g., Bermudez et al., *Toxicol. Sci.* 70: 89-97, 2002; Hext et al. *Ann. Occup. Hyg.* 46: 191-196, 2002). Of particular concern is the perception by this review of the failure of the authors to address adequately public comments raised during review of the 3rd External Review Draft concerning various animal and human studies cited in support of potential cardiac effects being attributable to PM.

As part of the review of the 3rd External Review Draft, CASAC asked that various dose metrics be presented for human to rat ratios to facilitate interspecies extrapolation of the animal toxicology results. This could be done in the dosimetry chapter or in the toxicology chapter. Table 4 from Miller (*Inhal. Toxicol.* 12: 19-57, 2000) is provided below and could serve that purpose.

Table 4. Human to Rat Ratios for Various Alveolar Region Dose Metrics^a

			***** Number of Particles per *****			
Diameter (: m)	Mass		Unit Area	Ventilatory Unit	Alveolus	Macrophage
	Total	Per Unit Area				
0.2	53	0.14	0.14	3.88	2.15	0.27
0.4	62	0.17	0.16	4.56	2.52	0.32
0.6	72	0.19	0.19	5.30	2.93	0.37
0.8	82	0.22	0.21	6.06	3.35	0.42
1	92	0.25	0.23	6.77	3.74	0.47
2	137	0.37	0.31	10.05	5.55	0.69
3	223	0.60	0.47	16.37	9.05	1.13
4	487	1.31	0.93	35.67	19.71	2.46
5	1197	3.23	2.09	87.81	48.52	6.06

^aAssuming monodisperse particles of unit density and adjusting for inhalability in the rat

Specific Comments

p. 7-33 The first paragraph makes the point that metals are at low concentrations in the ambient atmosphere and that metals found of concentrations less than 0.5 g/m³ were not reviewed in the previous Criteria Document. The authors then go on to state that more recently published data from high dose laboratory animal studies tend to indicate that particle associated metals are among likely potential candidates for inducing adverse effects attributed to ambient PM. The reader cannot tell from these sentences whether the point is the current draft will examine studies in metals that are found at low concentrations or that the studies that are presented based upon high dose exposures are still considered sufficient for implicating metals as contributing to adverse effects.

- p. 7-82, l. 15 This paragraph provides an excellent summary of the case for how there may be a neurogenic basis for particulate matter inflammation and should be included in the Summary section for the chapter to a greater extent than it currently is.
- p. 7-84, l. 20 In the discussion of the Lee et al. study, the point clearly comes across that instillation studies may be relevant to examining potential mechanisms but that these studies have to be approached with a degree of caution. Moreover, the authors should make it clear that, relative to risk assessment, inhalation studies should be the basis for using results from animal studies in extrapolating to humans.
- p. 7-87, l. 26 The sentence discussing rodent models of disease and stating criteria for judging the appropriateness of these models is not very useful in its current form. The authors should provide some examples of the issues.
- p. 7-94, l. 22 The description of the Kleeberger study discusses an overall magnitude of change being small and not being correlated with changes in macrophage phagocytosis. The dose used in this study of 10 mg/m³ carbon with 285 g/m³ of sulfate for a 4-h exposure of mice is a tremendous dose. The primary usefulness of this study has to do with the genes that were identified as potentially controlling susceptibility.
- p. 7-99, l. 17 The lead in sentence to this paragraph represents an overstatement of the results from the Diaz-Sanchez et al. study relative to extending the results for ambient combustion diesel particles containing particulate matter and their potential for significant effects on allergic asthma. The Diaz-Sanchez et al. study used 115 g of diesel particles in each nostril of the nose of subjects. To deliver any kind of comparable levels from ambient particles would require astronomical exposures. Thus, this paragraph while indicating a potential hazard is stating the potential in a much stronger context than warranted by the data.
- p. 126, l. 1 The description of the Nemmar et al. (2001) study using albumin nanocolloid particles instilled in hamsters provides some puzzling results. There is a temporal response at the 5, 15, and 30 minute sampling times, but the response at 60 minutes goes counter to this trend in a drastic manner. So the question arises, what is happening at 60 minutes? The results would indicate a time scale response of only a matter of minutes. What is the evidence for this from other studies? If none are available, then the study should be so noted as potentially representing a deviation of the likely time response pattern from particulate exposure.

9. Integrative Synthesis

General Comments

Overall, the authors have done an excellent job in this chapter of capturing the salient points contained in the preceding chapters, but the chapter is mostly a summary as opposed to an integrative synthesis of these salient points. The description of the legislative requirements and the sequence of events that EPA has entertained relative to particulate matter standards are useful and provides an excellent introduction to the chapter. The section on describing the organization of the chapter is also good because it sets the reader up for what is to follow. There are a number of areas for which the wording needs to be improved to provide clarity or for which there are technical errors in interpretation; these aspects are noted in the Specific Comments section below.

The Integrative Synthesis chapter does a good job of describing the types of endpoints that appear to be affected by PM exposure. However, there is currently no attempt to identify where the strongest case can be made for the need for PM standards in light of the various studies that have been conducted and no specific attempt to identify the appropriate indicator variable be that PM 10, PM 2.5, or PM 10-2.5. I believe that the addition of such a subsection to Section 9.9 would be most informative. In that regard, a quick tabulation of the studies reported in tables in Chapter 9 is given below for some of the endpoints. One quickly sees that PM 10 provides the most consistent indicator of various types of effects ranging from mortality to respiratory morbidity. PM 2.5 also does a reasonably good job for mortality and respiratory morbidity but is much poorer as an indicator variable for cardiovascular morbidity as is PM 10. In fact, for cardiovascular morbidity, PM 10-2.5 does almost as good a job as does PM 10. While I recognize that the table is a relatively simple one and does not account for various investigators analyzing the same city by different methods or over a different period of time, the point is that the data in Chapter 8 provide a wealth of information for attempting to identify the appropriate PM indicator variable and the level of that variable against which public health should be protected.

[See Table on page A-28 above.]

Specific Comments

- p. 9-11, l. 24 The acknowledgment is made that PM 2.5 includes some particles between 1 and 2.5 m Da from the lower tail of the coarse mode. The question arises as to the legal implications of this overlap relative to reaffirming or revising the current 2.5 standard and the possible introduction of a PM 10-2.5 standard.

- p. 9-11, l. 30 Text is provided that notes that size fractions are usually specified by a 50% cut point size. Specifically stated are the collection of 50% of 2.5 m particles and a rejection of 50% of these particles. Yet these particles are 100% inhalable in humans. Thus conceptionally the mass deposited in the human lung would be about twice what you would get if you used PM 2.5 monitoring samples. The question arises as to what change is needed in the concentration to capture the actual mass deposited in humans that represents the discrepancy between the penetration and inhalability curves if one is comparing equivalent exposure scenarios between animals and humans (i.e., extrapolating animal results directly is not straightforward for exposure concentration since inhalability and the sampler penetration curves must be taken into account.)
- p. 9-13 Fig. 9-5 provides a size cut curve for inhalable particulate matter that is labeled IPM. This curve does not match the experimental data of Breyse and Swift (*Aerosol Sci. Technol.* 13:459464, 1990). The curve has been generated from definitions given by the American Conference of Governmental Industrial Hygienists (1994). However, the experimental data should carry more weight and a fitted curve as available from Ménache et al. (*Ann. occup. Hyg.* 39:317328, 1995) should be at a minimum added to the figure or at best added and the IPM curve deleted.
- p. 9-20 Fig. 9-7 presents an interesting cartoon illustrating the particle bound water that should be removed as well as that which should be retained. Are there data from experimental studies that can assess the accuracy of the descriptive presentation? The appropriate removal of particle bound water is a topic that could influence whether or not cities are in compliance for various aspects of any PM 2.5 standard. Thus, this topic should be further discussed in the Integrative Synthesis chapter and to the extent that data are currently available, the text should be expanded. If data are not available to provide a range of uncertainty around the amount of water that is to be removed from the sample, this is an important research need that should be identified as part of the PM Criteria Document review process.
- p. 9-26, l. 4 The discussion here illustrates the amount of variability that can be present in annual mean concentrations. Typically annual mean concentrations are within 5 g/m³ of each other in urban areas but the spread in values can be much greater if consolidated MSAs (CMSAs) are considered. The statement that even with some MSAs those concentrations measured at separate sites on individual days can differ by over 100 g/m³ raises an important question relative to monitoring for compliance. Specifically, what does this description of variability say for limited sites being used to define compliance in any given city?

- p. 9-27 Fig. 9-9 shows concentration differences in three cities. It is interesting to note that 79% of the sites in Chicago, Illinois vary by less than 5 g/m³ so that one could contend that spatial variability is not an issue in Chicago. However, two-thirds of the concentration differences exceed 5 g/m³ for Detroit, Michigan. With these two cities as examples, the conclusion would be that the current standard of 15 g/m³ annual for PM 2.5 is potentially greatly affected by spatial variability in a city. This implies that an extensive monitoring network for compliance needs to be developed in order to accurately capture the annual exposure for some metropolitan areas.
- p. 9-30 The regression shown for daytime total personal exposure to PM 10 versus ambient PM 10 concentrations using data from the PTEAM study shows a very poor correlation coefficient (only about 14% of the variability in the data is explained). If this is typical, there is a potential difficulty in trying to use these kinds of curves for determining total personal exposure; looking at the variability of this parameter becomes important as it would have potential for identifying the extent of the population that might be affected by exposures to specified levels of particulate matter.
- p. 9-38, l. 20 The statement is made that there is still no published information that would suggest differences in exposure relationships for healthy versus sensitive populations. While these data may not be published, it seems intuitively obvious from the enhanced deposition of PM in these individuals compared to healthy subjects that individuals with pulmonary disease such as COPD have different activity patterns than normal healthy subjects.
- p. 9-40, l. 18 The authors need to be consistent in statements about sedimentation. In Chapter 6 (p. 6-6) sedimentation is described as important for particles greater than 1 m in aerodynamic diameter. However, in Chapter 9, the statement is that particles with an aerodynamic diameter greater than 0.5 m mostly are affected by sedimentation out of the air stream. There is a need to be consistent and to this reviewer, the Chapter 6 statement is the accurate one.
- p. 9-41, l. 18 Similarly to discrepancies on sedimentation, the authors refer to the coarse mode size range as being that containing particles greater than 1 m in size. However, in many other places in the Criteria Document the coarse mode is defined as particles greater than 2.5 m in size. This again points to the need for the Criteria Document to use a consistent definition of the different size range modes.
- p. 9-43, l. 11 The comments of this reviewer made about gender differences in Chapter 6 should be looked at and the changes brought forward to Chapter 9. Specifically, the comments made about the text on page 6-17.

- p. 9-43, l. 14 A number of statements are made about children showing particular effects in terms of particle exposure. The statement about greater total respiratory tract deposition in adults (possibly as much as 50% greater for those less than 14 years old than for adults greater than 14 years) is made and appears to be based on the studies of Bennett described in Chapter 6, p. 30. However, that result only applied to the 4.5 μ m particles. It does not hold for all particle sizes. For example, the 2 μ m experiments of Bennett showed no age dependency and no difference in total deposition between children and adults. A better description of the experimental data for children versus adults is needed in Chapter 9.
- p. 9-45, l. 3 The reference to CIIT as the Chemical Industry Institute of Technology is not correct. As the brochure for the MPPD model clearly indicates, the program was developed by the CIIT Centers for Health Research. In addition, the text should be modified to reflect the fact that the MPPD was developed by CIIT with partial funding from the Netherlands Ministry of Housing, Spatial Planning and the Environment.
- p. 9-46, l. 23 The statement that the clearance of particles from the alveolar region by alveolar macrophages and their mucociliary transport is usually rapid and is less than 24 hours is factually incorrect. The 24 hour clearance refers to the tracheobronchially deposited particles while the clearance for alveolar deposition ranges on the order of weeks to months or years. Even for a fast phase component of alveolar clearance, it would exceed 24 hours.
- p. 9-49, l. 24 The authors indicate the need for dosimetric calculations to accompany instillation studies to provide better information for human risk assessment. While this is certainly the case, it should be restated here that risk assessments should primarily be based upon results from inhalation studies given the problems discussed in Chapter 6 that are present in conducting and interpreting instillation studies.
- p. 9-69, l. 1 This statement is biased. To make the statement, one would have to assume that effects are present but there is no power to detect them. However, it is also possible that it could represent a true no-effect situation. The sentence needs to be modified to reflect the duality of potential interpretations.
- p. 9-69, l. 18 Remove ozone from the list of water soluble toxic gases as ozone is clearly poorly soluble in water.
- p. 9-76, l. 10 The statement is made that Table 9-8 focuses on various PM indicators and excess risk as derived from single pollutant PM models. It would be useful to indicate in this paragraph why single pollutant PM model results were chosen to

be presented as the basis for the table given that many of the authors also fit multi pollutant models.

- p. 9-91 Table 9-10 represents an important table describing cardiovascular and respiratory related morbidity effects size estimates. It may be useful to use this table to develop another table that would provide the indicator level and then the effect type with the proportion of studies being significant out of the total number described.
- p. 9-136 What does the * mean in Table 9-13?
- p. 9-137 Figure 9-23 does not relate to nor have implications for dose unless one assumes the same deposition fraction for children and adults. And we know based upon results presented in Chapter 6 that this is not the case. There is limited value in retaining this figure.
- p. 9-139 Section 9.10 has no references provided in the text in contrast to other sections in Chapter 9. In addition, the material that is included is speculative and includes only a general description of potential changes. This makes the section of limited value. What specific environmental effects that can be ascribed to PM should form the basis of the section.

Mr. Richard L. Poirot

Fourth External Review Draft of Air Quality Criteria for Particulate Matter (June, 2003) CASAC Review Comments from R.Poirot, Assigned Chapters: Exec. Sum., 1, 2, 3 and 4 General Comments

Chairman Hopke has emphasized the need for some expediency – to reach closure on as many sections as possible and to further consider whether an additional round of review is needed. I also looked for “responsiveness” to comments previously submitted, and tried to envision an “EPA staff perspective” (will staff be sufficiently well-armed with the information presented in the CD to proceed with the challenging next step of reviewing and perhaps revising the current PM standards?).

Generally I found that EPA was quite responsive to previous comments, and has made other additions and revisions that make this a much better document. I’ve submitted additional comments, almost all of which are minor, and (considering the responsiveness last time) do not believe an additional review is needed for Chapters 1-4. My only “major” comments relate to a relatively minor topic area (relation between PM and visibility) where I think the document (is much improved from last time but) could still be strengthened. I’ve also attached some “supplemental comments” on visibility that I submitted after the last CASAC review meeting, in the event that these did not get conveyed last time.

Executive Summary

p.E-4, para 1, line 4: Change “while recognition” to “with recognition” or “while recognizing”.

p. E-5, para 8, line 7 (and generally elsewhere)” Suggest changing “...the Positive Matrix Factorization technique...” to”the Unmix and Positive Matrix Factorization techniques...” PMF is a good receptor model in skilled hands, but so is Unmix.

p. E-7, para 12, line 6: Suggest changing “... efficiency of retention...” to artifactual losses or gains ...”. If the HNO₃ denuder malfunctions, one could experience positive NO₃ artifacts on nylon filters, and a substantial positive OC artifact is, I think, relatively clearly recognized on the quartz filters from the STN network. NH₄ is also subject to positive sampling artifacts in current routine networks. These positive artifacts definitely can mess up your source attribution and epi studies. A somewhat related point (that I don’t think needs to be in the summary, but which relates to the emphasis on artifactual sampling losses) is that indoor NH₄NO₃ concentrations likely diminished relative to outdoor due to absence of indoor HNO₃ and resultant shifts in HNO₃/NH₄NO₃ equilibrium, so there may be a certain coincidental parallel between artifactual losses of volatile NH₄NO₃ in continuous and FRM filter sampling and total human exposures.

p. E-36, para 4, lines 1&2: I don't like the wording of these 2 lines because:

- "less of both types of information" has no coherent meaning (what information?).
- "mass and composition" is wrong. If you have composition you don't need mass.
- Knowing composition alone (without also knowing or estimating or assuming ambient RH) provides little additional visibility information beyond that provided by mass. The water/mass adjustment is (at most times & places) by far the most important visibility information inferred from the species information.

Light extinction and the true ambient mass of fine particles are very nearly the same thing, and you might say that the difference between visibility and measured PM_{2.5} is primarily the water that we deliberately remove from the ambient aerosol with our proscribed FRM methods.

Meanwhile, measured PM_{2.5} alone is still an excellent indicator of visibility effects (a better indicator of visibility than it is of any other effects considered in this CD). A suggested revision to this bullet is:

There are several quantitative indicators of visibility, including: (a) fine particle mass or fine particle composition (both of which are strong indicators alone but could be refined as indicators by adjusting for or screening for ambient RH), ..."

2. Physics, Chemistry and Measurement of Particulate Matter

p. 2-28, lines 10-12: Might revise to "... organic compounds; crustal material; and (at coastal locations) sea salt".

p. 2-41, line 17: "Change "sales" to "salts" or "species".

p. 2-51, line 6: could add at end ", or from errors in assumptions regarding unmeasured "associated species".

p. 2-52, line 10: Change "that" to "than".

p.2-59, lines 20-26: (an editorial comment only, but) The cautionary caveat that these studies featured collection and extraction of samples immediately after sampling is well taken. Typically, in most "research-grade" studies where immediate, post-sampling sample collection, extraction or refrigeration is employed, the sampling schedule is also different from the midnight to midnight schedule employed in most routine filter networks. For example, 8 AM to 8 AM is common (not sure what was actually used in SCAQS). Often the importance of fast postsampling filter treatment is emphasized, while the artifact-minimizing effects sampling schedule are ignored. Midnight to midnight filter sampling is an excellent way to lose (early morning peaks in) semi-volatiles from filters during sampling, and should be reconsidered in our major networks.

p. 2-60, line 16: I thought it was a Na₂CO₃-coated "filter", not "denuder" downstream of HEADS
Teflon filter? Petros?

p. 2-62, lines 24-28: Approximately the same caution on denuder effects on gas/particle equilibrium shifts mentioned here for SVOV, could also be mentioned for denuded nitrate sampling (but isn't).

2-64, lines 22, 23 and generally in this "continuous" section: Some of this summary is a bit out of date. For example, a substantial fraction of current TEOMs are not run at 50 deg C, but at 30 or 40 with Nafion dryer. Nor is the RAMS (p. 2-66) the only continuous method to employ a Nafion dryer. Advances have also been made in the various "smart heaters" in several of these methods, but are not discussed here.

p. 2-84, line 6: Not sure of exact date, but I think the IMPROVE Network (or at least most sites) changed from 2 samples/week (wed & sat) to 1 in 3 day sample schedule in the Fall of 2000.

p. 2-87, line 22: suggest changing "assumptions" to "assumptions and analytical procedures". You can assume anything; it's the procedure that makes the difference.

p. 2-87, line 28: Could change "be burnt to" to "lead to the formation of". Non-combustion-related OC precursors can also lead to pyrolyzed OC during thermal analysis, both by forming organic aerosols and/or by forming organic artifacts on (and through) quartz filters.

3. Concentrations, Sources and Emissions of Atmospheric Particulate Matter

p. 3-32, lines 24 & 25: I suspect, but don't know, that most of those (few) occurrences with $PM_{2.5} > PM_{10}$ were likely at very low concentrations. If so, this might be worth mentioning (as I think the "horrors" some attribute to the difference method are overblown).

p. 3-37, line 21: If Co, As & Se were "not detected" in the coarse samples, then what's the meaning of the correlations for these reported in tables 3-2 & 3-3?

p. 3-54, line 27: Change "were" to "was".

p. 3-62, lines 27 & 28: "especially during the warmer months" is true for sulfates, but not for nitrates – predominantly a Fall-Winter aerosol species.

p. 3-63, line 21: could add "the sources, trends and" before "possible environmental effects of NH_4NO_3 ."

p. 3-73, line 12: Few of these receptor model techniques described here actually utilize the "time series" information in these data (ie. The temporal sequence of samples is irrelevant). Maybe could change this to "rely on the varying mix of species present in multiple observations of compositional data".

p. 3-88, line 2 (and elsewhere): could add “and Unmix” after “PMF”. PMF is not the only model of this type.

p. 3-88, line 11: Song et al. (2001) characterized their wood smoke sources at Brigantine and Underhill as “connected with local residential wood burning and occasional forest fire impacts”. So you should change “wildfires” here and on 3-89, line 3 to “wood smoke”.

p. 3-102, line 18: Could add “as well as by the detail and quality of ambient measurement data” after “availability of source profile data”.

4. Environmental Effects of Airborne Particulate Matter

p. 4-8, line 1: Could insert “local” before “nitrogen deposition”. Aerosol formation doesn’t eliminate deposition, it merely delays it.

p. 4-8, lines 10: Same as above, could add “in the vicinity of emission sources” after “vegetation”.

p. 4-8, lines 15 & 16: This “emissions of cations have increased” (since 1990) is a bold statement, and needs some documentation (if its true). Over what geographic scale?

p. 4-71, lines 11 & 12: This is at least the 3rd repeat of the “benefit to vegetation” of gas/particle conversion, and I think it should again be indicated that this benefit is only to local vegetation (and/or point out that the effects of concern being discussed here are only those resulting from direct foliar exposure. By coincidence (or “geology”), areas with highest SO₂ emissions (with abundant deposits of high-sulfur coal) also tend to have relatively deep, well-buffered soils, while thin soil (mountainous or Precambrian Shield) areas further downwind can have much lower tolerance for sulfur deposition. If no gas/particle conversion occurred (an absurd hypothetical), sulfur deposition would be substantially increased locally and decreased downwind, and that would clearly benefit vegetation in those poorly buffered downwind areas.

p. 4-86, lines 5-14: This discussion of acidic deposition effects is rather minimal, and includes by reference, publications which are 10 to 20 years old. I think you might either include references to a few more recent references, indicate that more detailed discussion will follow (it does), or maybe just leave it out. Generally, this chapter is not well organized (keeps circling back around to similar topics). This makes for awkward reading (& reviewing), but is not a critical detriment, so long as the material is covered and the repeated discussions are not contradictory.

p. 4-157, line 4: suggest changing “causes” to “often contributes to”. Light absorption by carbonaceous particles and some crustal particles can also contribute to urban “brown clouds”.

p. 4-161, line 1: I assume this range of scattering efficiencies for “sulfates” excludes effects of associated water, else the range could go much higher. Could add “dry” before “scattering”, or maybe preface this with a few sentences explaining what “scattering efficiency” actually means (per unit mass of what? At what wavelength(s)?).

p. 4-167, lines 1-9: This “reconstructed extinction” equation (4-8) is essentially repeated on p. 4-170 as equation 4-12, but the equations differ, and neither is quite right. This one needs “(NH₄)₂SO₄” changed to “NH₄NO₃” in line 6 and lacks an explanation of “b_{Coarse}”. Also b_{OC} is not really 4(OC) its 4(OMC) or “organic matter” or “organics”, where OMC (organic matter by carbon) is typically (though not always accurately) estimated as 1.4*OC.

p. 4-168 (and generally in this section): The emphasis here seems to be too much on the deviations in the (fundamentally strong and causal) relationship between fine particles and visibility, rather than on the strength of that relationship (which could be refined but not substantially be altered by consideration of more complex contributing factors). It sounds almost like EPA has predetermined that consideration of any sort of secondary PM standards for which visibility protection is a goal, is something to be avoided. My concern here is only that sufficient information be contained in the CD (or by reference) to allow EPA to consider (and potentially justify) the option of a secondary PM standard (or for that matter to help justify a shorter averaging-time primary standard if such a standard is otherwise warranted). Some examples:

p. 4-168, lines 7-9: True, as indicated, that measurement and separate treatment of fine particle chemical species can provide a better indicator of visibility than mass alone, but this improvement comes primarily from calculations of associated aerosol water, and so requires measurements, estimates or assumptions about concurrent ambient RH in order to represent much of an improvement over fine mass alone. One could conceivably do nearly as well with a fine mass indicator if a similar “generic empirical” f(RH) function were applied to those data (or if filters were reweighed under the specific RH conditions encountered when they were being collected - although I don’t recommend either approach). The difference between light extinction and fine particles as we measure them lies almost entirely in the contribution of associated aerosol water – which we deliberately remove in our operationally-defined FRM methods.

p. 4-168, lines 9-12: True again, as cited from the recent Chow et al. (2002a) analysis that light scattering measurements may be useful indicators of short-term PM_{2.5} variations under dry conditions. But this understanding is hardly unique or recent. There are at least 3 different nephelometer designs currently employed as continuous PM_{2.5} monitors in various state and local networks, one of which typically employs only a light bulb for heating and has no size-selective inlet, but functions quite well in the Pacific Northwest.

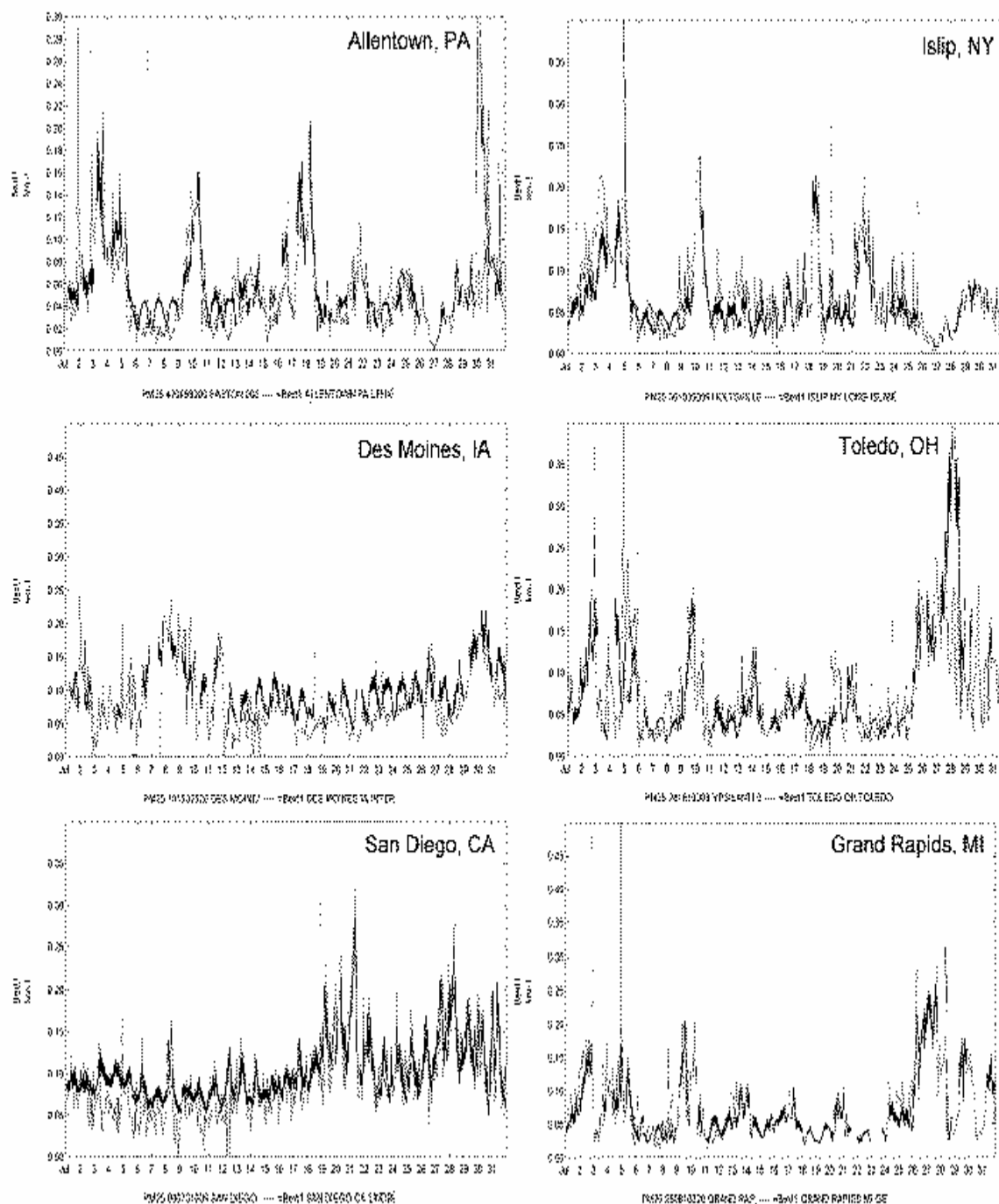
p. 4-168, Lines 11-12 and Fig. 4-37: This is the only information in the entire CD that indicates a quantitative relationship (4m₂/g) between fine mass and visibility (light extinction). The citation to Chow et al. (2002b) is accurate, although it was taken specifically from Warren White’s section of that review article, and was cited there to 1970-71 data from Samuels et al. (1973),

and presented to illustrate the point “that some researchers had already associated haze with fine particle mass by the time of the original 1970 CAA.” This (old) quantitative extinction to mass relationship of $4\text{ m}^2/\text{g}$, is quite close to the lower bound ratio derived from reconstructed extinction and measured fine mass from the more recent IMPROVE data (figure 16 in your cited Chow et al. (2002b) paper), which is quite logical considering that the Samuels et al. data were from relatively dry (and low sulfate) Los Angeles, and further limited to (less humid) daytime hours with RH constrained to $< 70\%$. This figure (16) also shows an upper bound of about $8\text{ m}^2/\text{g}$ for the IMPROVE fine mass data. See also my supplemental comments from last time based on a larger set of the IMPROVE data, which indicates an approximate average relationship of about $6.5\text{ m}^2/\text{g}$. Using this empirical relationship a visual range of 10 miles (the visibility level at which California has considered air quality to be “adverse” – since 1959) would be equivalent to a $\text{PM}_{2.5}$ concentration in the range of 30 to $40\text{ ug}/\text{m}^3$ (similar to the level of the Canadian short-term $\text{PM}_{2.5}$ health standard of $30\text{ ug}/\text{m}^3$). A visual range of 10 miles (quite noticeably hazy compared to clean air) is also the level at which the NWS starts reporting impaired visibility for purposes of aviation safety. Since visibility is a short term (instantaneous) effect, and since the current US short-term $\text{PM}_{2.5}$ standard of $65\text{ ug}/\text{m}^3$, 98th percentile is extremely hazy (about 5 miles), but rarely violated, we could observe that virtually the entire range of current adverse effects on visibility lies unprotected below the level of the current $\text{PM}_{2.5}$ standard.

The following figure, taken from a recent evaluation of (raw, uncensored) ASOS visibility data by R. B. Husar compares “humidity-adjusted” light extinction with continuous $\text{PM}_{2.5}$ mass measurements for 6 sites in different regions (which presumably have different aerosol compositions). The RH adjustment involved screening out periods of humidity $> 90\%$ and then applying a generic (inverse) $f(\text{RH})$ function – based on an assumption of consistent hygroscopicity in the aerosol mix at all sites. The $\text{PM}_{2.5}$ data are not collocated, merely in the same urban areas, yet the correspondence is remarkably strong at all sites.

Comparisons of (Humidity Adjusted) ASOS Visibility data and "nearby" Continuous PM-2.5 Mass

from: Evaluation of the ASOS Light Scattering Network, Progress Report, May 2002,
Submitted by R. B. Husar, CAPITA to James F. Meagher, NOAA Aeronomy Laboratory



Dr. Frank Speizer

Comments for CASAC on Chapter 8

Page 8.5 Definitions of prospective cohort (and panel study). This is an oversimplification. There are distinct differences between a prospective cohort and a panel study (mostly size and therefore the actual amount of data possible to collect in each case).

Page 8.5, Definition of case control. The example of an occupational study is inappropriate. It is more like a cohort study than a case control study. Suggest leave out.

The discussion contained in section 8.1.3, is rather textbook and very reminiscent of text from previous Criteria Documents. It seems to me that it would no longer be necessary to include this exposition of roughly 5-10 pages in future Criteria Documents and those who are using this report certainly know it already and if they don't they never will use it or understand it.

Page 8.120—Concern about the way CD introduces and takes account of the GAM problem. The impression here is that a number of studies are being left out, where as the fact is that later on in the chapter in almost too much detail each study is reviewed and compared with and without GAM correction. Much of what is being reported was summarized in the HEI report. Need to mention it.

Page 8.149 The same issue is again raised regarding the GAM function. Here authors say that those studies that used the restricted GAM for respiratory disease are simply going to be left out. I hope that again this is not the case.

Page 8.159 and perhaps a few pages before: The author lapse into quoting the author of the article directly. Not clear that this is wrong, but stylistically it indicates a different author is writing this section.

Page 8.172-3 and perhaps elsewhere

Particularly in tables but also in text there is considerable variation in calculating risk estimates by using different standardization values for calculating risk. E.g. 50ug/m³ vs 25ug/m³. Results might be more comparable if used same values.

Page 8.192-204 GAM discussion good. Covers issues and presents results fairly.

Page 8.204-218 Confounding by Co-pollutants. Presentation is exhaustive and exhausting. Could have said in lot fewer words, and simply raises imponderables. As long as we set standards on a pollutant-by-pollutant basis these problems will remain. What is not got at is effects of modification of effects of PM by co-pollutant nor could they be with the kinds of studies that currently exist. This does as good a job as can be done, but will open CD to criticism by those who want to be critical rather than constructive.

Particulate components

Lags

Concentration-response relationships

Heterogeneity of PM effects estimates—33 to over 80 studies

There is a certain amount of redundancies in this chapter, which could be edited out. However, overall the chapter does a good job in covering a complex field. In several places the authors wander into territories they just as well should not have explored. They speculate on the role of epidemiology and that speculation will simply become ammunition for those who will say that epidemiology can never prove anything. They would have been a lot better off if they simply used Hill's postulates to test the coherence and other properties of the combined results.

Appendices are simply packed with data. It would be useful to recommend that these data be put into a searchable database for future use. Rather than doing anything more on the chapter CASAC should recommend that the next effort be to do that rather than further tinkering with the text.

Response to Moogavkar review

Dr. Moogavkar raises a number of important issues that will need to be responded to. For the most part they are accurate statistical facts related to his own analyses and his assessment of the statistical aspects of the air pollution literature put forward since 1996. I agree with some of his argument that we are in fact dealing with a complex mixture in which PM may only be a surrogate for the mixture in the air. I would take issue with his consideration of SO₂ as a potentially more important pollutant when found in conjunction with PM simply on the basis that it is of greater statistical significance in any given analysis.

He reduces the 18 conclusions (I did not recount them) to one.

If one were to do that I would have to add the following to his one conclusion:

In many of these studies PM with and without added components of gases appear to be the putative agents. From what is known about the toxicology and clinical studies about the gases, performed for the most part prior to 1996 and thus not reported in detail in the current CD, it is clear these gases do not carry sufficient biologic plausibility to substantially affect the results seen. SO₂ simply does not travel beyond the upper airways under normal breathing condition and although it might reflex affect airways to contribute to asthma exacerbation it cannot have effects on COPD or CVD to contribute to excess morbidity and mortality. Similarly, because of lack of correlation separating the effects of PM from O₃ seems justified on the basis of simply adjusting one for the other. The same may not be said for some of the other major gases pollutants. It is also the case that the most consistent findings from the heterogeneity of studies done in different sites is that the PM signal comes through most often.

Surely the totality of the health effects result from the mixtures, and thus it is prudent to take steps to reduce exposures. In fact the law requires EPA to do that and to do it with an adequate margin of safety. Therefore it is prudent to acknowledge that by reducing PM from combustion sources other potential putative agents will also be affected in a direction that would reduce their health impacts as well.

Table 9.10 The problem with this table as a comparison between PM10, 2.5, and “course thoracic” is not intuitive because it uses different multipliers for each. In particular in trying to separate PM10 from PM 10-2.5 it is not intuitive to compare risk for 50ug in one and 25 ug in the other.

Many of the comments suggested by “public” which in fact represent consultants for vested industries, are in fact restatements of many of the caveats presented in the discussion to the findings presented in the CD. These statements are turned into concerns that give the appearance that the writers of the CD have not considered these comments from previous drafts. I do not believe this is the case and for the most part the staff can respond, if at all, by referring to the relevant section of the document.

Dr. George E. Taylor, Jr.

G. Taylor
School of Computational Sciences
George Mason University
25 August 2003

This review is limited to the topics of ecology, natural resources, climate change and visibility. It includes the relevant chapter on welfare (Chapter 4), Executive Summary and Integrated Synthesis (Chapter 9). It is noted that some of the concerns raised earlier have been addressed (e.g., inclusion of welfare issues in the Executive Summary; EPIC report) but the majority have been left without comment.

The prevalent and pervasive lack of focus in the welfare issues associated with PM remains the single most important issue. The document and Executive Summary fail to focus on the issue of PM and ramble without organization on the key issues of exposure and response. As a consequence, the document fails to present the information needed to evaluate the risk due of PM for welfare effects, either herein or in the Staff Paper. The document contains a tremendous amount of information but most of the information is tangential to the charge of PM. The most glaring problem is the obsession with nitrogen. Nitrogen is not synonymous with PM and other CD's address the nitrogen issue. In fact, the PM section for human health has little reference to nitrogen, and there is very little discussion of nitrogen in the atmospheric section. The lack of focus strips the welfare section from having a role in the NAAQS. In my judgment, the PM CD for welfare could be collapsed into fifty pages if the risk format was adopted and the organization tracked PM *per se*. This same argument was made in the last review.

In my view and based on the CD presented, there is little argument for conducting a PM risk for welfare effects and the organization of the CD – disorganized and unfocused - confirms that position.

In light of the above, it is illustrative to compare the quantitative and risk based approach (exposure and response) used to address human health with the diffuse and largely irrelevant discussions to address welfare effects. .

Executive Summary

This section on welfare is new so this is the only opportunity to offer comments. The following are noted:

1. What is the objective of the PM CD with respect to welfare effects and how does that objective compare with that devoted to human health?

2. The focus on nitrogen is inappropriate in this CD. There is essentially no discussion of nitrogen in the exposure section which precludes any discussion in this section. An organization around the risk model of exposure – response would have been appropriate.
3. The front end of the summary is largely an Ecology 101 primer and is so simplistic as to be uninformative. As a point of comparison, the section addressing human health is chocked full of state of the art science. The science underpinning ecology and natural resources is far more sophisticated than the CD gives credit. Plus, many of the statements are simply untrue because of the generality. I encourage OAQPS to recognize that it needs to be an advocate for ecology, natural resources and the environment. Within the Agency it is important that OAQPS have a commitment to ecology rather than viewing it as a necessary evil.
4. Editorial problems are commonplace in this section and it is recommended that the CD be reviewed by an editor.
5. The most significant finding in the summary for the biology community is the creation of an entirely new taxon of actinomycetes as being distinct from the fungi.
6. The argument that the “soil is the most dynamic site of biological interaction” (page E-30) is an interesting statement but clearly no one can argue that case; this is simply a misstatement and suggests a lack of critical understanding of all of living systems, all of which are complex and interaction. I would not begin to prioritize one (i.e., soils) as being more interactive as any other (e.g., neural networks in the brain, functional genomics in the DNA, hormone signals and effectors in living systems).
7. The argument that “few heavy metals have been documented to have direct phytotoxicity under field conditions” (page E-34) runs in the face of all of the literature. There is in excess of 1000 articles in the literature that address heavy metal effects on plants under field conditions. This paragraph has numerous editorial and logic flow errors.
8. The section on phytochelatins (page E-34) is unlinked with the exposure section of the executive summary (same problem as with nitrogen). This chapter needs a dose of logic and syntax editing.
9. The section on nitrogen needs to be re-written as there are serious concerns with respect to its authenticity and source.

Key conclusions for the CD are presented on pages E-40-44. There is no mention of any welfare issue as being a key conclusion. Based on Chapter 4’s organization (academic model versus a risk based organization of exposure and response) and the inappropriate preoccupation with nitrogen, I would agree that welfare issues should not be carried forward.

In summary, this section fails to address the issue of PM and welfare effects.

Chapter 4. Environmental Effects of Airborne Particulate Matter.

1. The title of this section is specific to PM and yet the Chapter is largely focused on nitrogen. Maybe a statement of the objective of this section is in order to foster some focused organization. On page 4-2 there is a two phased statement of the objective, but again there is no reference to nitrogen.
2. The discussion of ecological attributes from the EPEC report is appropriate reference.
3. In a technical sense, the majority of the information in the CD is characterized appropriately.
4. The section on nitrogen needs to be re-written as there are serious concerns with respect to its authenticity and source.

Dr. Sverre Vedal

August 25, 2003

Critique of 2003 PM Criteria Document draft

Chapter 8 (Epidemiology)

1. Fairness/objectivity.

The tone of this chapter has improved, in the sense that it now appears to be less of an attempt to convince the reader of a certain point of view, and more of a balanced review and appraisal of the relevant literature. The CD does a better job of living up to the promise of attaining the “goal of producing an objective appraisal of the evidence, including weighing of alternative views on controversial issues” (p.8-4, L8). More qualifiers are included when appropriate, and there is more indication that many findings are sensitive to modeling choices. For example, the relative effects of fine and coarse PM (pp.8.109-110 & 233) are presented with more objectivity, although there is still a tendency to attribute coarse PM effects to peculiarities of coarse PM composition, as if fine PM is immune from these considerations. The description of the Lipfert cohort study is more fairly described (p.8-109 & 114), as is the section on harvesting (p.8-273). The conclusions regarding harvesting are appropriately conservative (p.8-273, L15). There is some unevenness of tone, possibly reflecting the patchy nature of the revisions, with some non-revised sections still maintaining the original stance. For example, the section on respiratory hospitalizations carries on in the vein of the earlier versions (see #6 below), as does the section on heterogeneity of effects (see # 10 below).

2. Confounding and the gaseous pollutants.

In my opinion, the possibility of residual confounding remains the principal impediment to fully accepting the PM-health outcome associations as being causal. It is therefore appropriate for the CD to include a section on principles of confounding, with application to time series studies, specifically. It is clear that the motivation for this effort is largely to call into question the legitimacy of viewing the gaseous pollutants as confounders. The basic argument is that a confounder must be an independent cause of the outcomes of interest. Several tacks are taken to argue that the gaseous pollutants do not fulfill this requirement. First, it is argued that since ambient measurements of the gaseous pollutants do not reflect personal exposure to the gases, ambient gaseous pollutants cannot cause the outcomes, and therefore cannot be confounders (p.8-10, L12; p.8-9, L6; p.207, L6; p.8-211, L3). This argument ignores what seems to be obvious: namely, that the ambient gaseous pollutant concentrations are surrogate measures of some time-varying phenomena. If these time-varying phenomena affect health, which they seem to do, then there is justification for considering the gases as measures of truly confounding factors. Use of surrogate confounder measures is not unusual in epidemiology. For example, we have little difficulty in considering socio-economic status, or level of education, as potential confounders, even though neither can be considered a direct cause of a health outcome. They are merely surrogate measures of factors that are true confounders. In the same way we

can consider gaseous pollutants as surrogate measures of true confounders that are poorly understood, or cannot be measured directly. Note, we also seem to have little difficulty in ascribing “effects” of carbon monoxide or sulfate to sources or pollutants for which they are surrogate measures, so the notion of surrogate measures is not a foreign one. Few argue (although some persist in doing this) that the apparent effects of CO or sulfate are due to the direct effects of these pollutants.

Second, it is argued that some gaseous pollutants might be considered to be part of the causal pathway in which PM causes adverse effects, and should therefore not be considered confounders. If this were true, then the gases should correctly not be included in PM models. A pathway for formation of PM is presented (p.8-204, L28) in which NO forms NO₂, which in turn forms nitrate, which then contributes to the PM mass. This implies that the only effect of the gases (in this case NO₂) is through the formation of PM. I do not find this argument compelling, since the effects of the gases on health do not require that they act through this pathway.

I find some inconsistency in how the role of gaseous pollutants is represented. An argument is made (see above) that the gases should not be considered as confounders. However, in many later presentations of PM effects and their sensitivity, or lack of sensitivity, to inclusion of gaseous co-pollutants in the models, this issue does not come up. Especially in the section reviewing morbidity effects, findings are presented from models in which variables for gases are typically included in the models to address the matter of confounding by the gases. While I believe that concentrations of gases do measure important confounding factors, likely as surrogate measures (see #1 above), the presentation of multi-pollutant model results is confusing without acknowledging again the controversy as developed on pp.8-8, 9, & 10.

The attempt to assign to the gaseous pollutants a role as surrogate measures of aspects of PM (p.8-206) is, I believe, as step in the right direction, in the sense that it admits to the possibility that gases (and ambient concentrations of any pollutant, for that matter) are surrogate measures. However, I don't believe there is evidence that gases are exclusively measures of aspects of PM, and in fact may not be primarily measures of PM at all. Instead, it seems likely that the gases are acting as measures of some features of the time-varying atmospheric phenomenon that includes the complex interplay of pollutants and meteorology. There is no good reason why PM should also not be considered a surrogate measure of some aspects of the same phenomenon. The tendency to interpret effects from models in terms of the names of the variable measures is an unfortunate, and naïve, practice.

3. GAM issue.

The issues regarding the impact of use of the default convergence criterion in GAMs have been reasonably well handled. There seems to be an implicit assumption (p.8-9) that estimates of effect from those studies that had not used GAMs are unbiased. It should be pointed out that, although these studies were not plagued by poor estimate convergence, effect estimates from these studies may be as sensitive to degree of temporal smoothing and specification of weather as any study that used GAMs.

There does not appear to be any general review, however brief, in the text of new/revised findings of single-city studies. There is a brief introductory section (8.2.2.2, p.8-23), and a section devoted to the new multi-city studies (section 8.2.2.3, p.8-30), but nothing about any general impact of the single-city studies, apart from listing them in Table 8-1.

4. Chronic effects.

The presentation and discussion of studies of chronic PM effects is reasonably balanced and indicated issues, such as that of spatial correlations (p.8-86), that are not fully resolved, and model sensitivities, such as sensitivity to inclusion of time-dependent PM measures. One aspect of spatial correlation that is confusing, and I'm certain that there are others, is the relationship between spatial correlation and confounding. There is a suggestion in the CD that accounting for spatial correlation will address potential confounding due to unmeasured factors that are spatially related to pollution and mortality (see p.8-95, line19 [section 3, 2nd sentence], for example). I don't believe that is true, in the same way that accounting for autocorrelation in time series studies does not address confounding due to time-varying confounders. Therefore, while accounting for spatial correlation is important, adequately accounting for it does not provide assurance that effect estimates are unconfounded.

If you decide to consider more recently published papers, the paper by Hoek et al. on Dutch mortality would be high on the list.

5. Presentation of results (e.g., best lag).

I would have thought that the issue of reporting only "best lags" has been laid to rest, particularly given the work of Lumley and Sheppard (p.8-234). When best lags are used to indicate the range of estimated effects, such as in Figure 8-12 (p.8-137) for cardiovascular hospitalizations, and when "the maximum lag model" (p.8-149, L14) is used for estimating range of effects for respiratory hospitalization, the range is biased upwards. The statement, "While this practice [use of best lag] may bias the chance of finding a significant association, without a firm biological reason to establish a fixed pre-determined lag, it appears reasonable" (p.8-234, L15). Since when is it reasonable to use effect estimates known to be biased? While it is true that there is often no good biological reason for preferring one individual lag over another, this in no way supports use of a biased effect estimate.

Another example that demonstrates an unfortunate tendency to selective summarization of results pertains to the conclusion that the results of the reanalyses of respiratory hospitalizations did not substantially affect conclusions. Zanobetti and Schwartz (2003) reported revised findings on pneumonia hospitalizations from the 14-city study. In Table 8-17 (p.8-150) and Table 8-18 (p.8-152) one gets the impression that effects were still present, even using GLM and natural cubic splines. Unfortunately, this effect is only present for lag 0 or the mean of lags 0 and 1; for all other lag formulations, including the distributed lag, arguably a preferred formulation, the previous effects disappeared (see p.51 of the HEI Special Report, Revised

Analyses of Time-Series Studies of Air Pollution and Health, May 2003). At the least, these findings indicate extreme sensitivity of the pneumonia findings to approaches to smoothing. Such selective presentation tends to weaken the overall impression that this version of the chapter is more objective and balanced than previous versions (see #1 above).

6. Meteorology.

I would dispute the statement, “The time-series studies published since 1996 have all controlled adequately for weather influences” (p.8-146, L18). This issue of the specification of meteorology in the regression models has again raised its head in the aftermath of the GAMs convergence problem. The sensitivity of findings to weather specification is again an active area of work. As evidence that the debate over the correct specification of meteorology continues, an attempt is made to attribute the smaller effect estimates from NMMAPS to mis-specification of meteorology effects (p.8-48-49). It is perhaps equally likely that larger effect estimates from other multi-city studies are due to mis-specification of meteorology in those studies.

7. Susceptibility.

While this discussion (section 8.3.2.5, p.8-165) is generally well done, I point out that studies addressing susceptible subgroups seldom include a direct comparison among different subgroups within a single study, and therefore do not directly address the issue of susceptibility. Therefore, statements such as, “...the elderly are especially affected by air pollution” (p.8-166, L9) and “The groups identified in these morbidity studies as most strongly affected by PM air pollution are older adults and the very young” (p.8-168, L5) need to be weakened.

8. Intervention studies.

Presumably because of the deadline for inclusion of published studies, some important recent “intervention” studies, notably the Dublin and Hong Kong mortality studies, were not included. This is unfortunate, since these have direct relevance to the PM CD, and like most “intervention” studies, avoid some of the weaknesses of the other types of observational studies reviewed. I would take exception with the strength of the statement, “Taken together, these epidemiologic intervention studies tend to support the conclusion that reductions in ambient air pollution (especially PM) exposures resulted in decreased respiratory and cardiovascular health effects” (p.8-218, L11). For Atlanta, a primary role for ozone is as likely as that for PM, and for East Germany and especially Hong Kong, the evidence is more compelling for a role for SO₂ than for PM.

Regarding the “intervention” studies that are reviewed, I believe that the summary of the Utah steel mill closure studies is incorrect and needs to be changed (p. 8-214, L24). Only the published study of monthly hospitalizations used the period of steel mill closure in the design and analysis. The study of mortality, lung function, symptoms, and school absenteeism used traditional time series or longitudinal panel study designs to evaluate daily effects of short-term changes in PM concentrations, and did not explicitly investigate the effect of the steel mill closure. The summary in the CD indicates that all of these health outcomes were part of the “intervention” study, when in fact they were not.

The discussion of the Atlanta Olympics study (p.8-155) should add a qualifier, as in the discussion of the Utah steel mill closure, that it is possible that other factors associated with an Olympics might have confounded what appear to be pollutant effects. It could be argued, if possible, that these factors are unlikely to confound, supporting the conclusion that “this study supports the hypothesis that ...”. The similarities of these “intervention” studies to experimental studies (as suggested by the term “quasi-experimental”) can appear to be greater than in fact they are.

9. Threshold.

The discussion of the threshold issue is adequate. I would suggest that while the finding of a U-shaped or V-shaped PM concentration-response relationship in the Smith study in Phoenix is “difficult to interpret biologically” (p.8-240, L31), it could be explainable if PM is serving as a surrogate measure of some aspect of meteorology.

10. Heterogeneity.

The discussion of heterogeneity of effect estimates in NMMAPS is, I think, misleading, and sometimes incorrect. On further inspection of the plots derived from NMMAPS in which city-specific effect estimates are ranked by a measure of power, the so-called “funnel” plots (pp.8-244, 245), I find little evidence to support the contention that cities with higher power tend to show consistently positive estimates of effect. In fact, of the 8 cities with the most power, 2 show no effect (one slightly negative), 3 are substantially below the already low mean estimate of effect, 2 are just below this average, and 1 (NYC) is substantially higher than the average. I find no consistent message there. Obviously the precision of the estimates narrow as power increases, but a figure isn’t necessary to make that point. It is incorrect to state that “many [effect estimates are] statistically significant” (p.8-243, L27; p.8-246, L4 & L10), since only that for NYC and Oakland, of all the 90 cities, is positive and statistically significant. Further, the impression of objectivity is hampered by drawing particular attention to the estimate of effect for Oakland (Fig. 8-22, p.8-245, L11) in the group of “Northwest” cities, just because it happens to be larger than effects of the other cities with high power; 4 cities in the Northwest have greater power than Oakland. The characterization of effects for industrial mid-west cities with the most power as “positive” (p.8-246, L4), while strictly true, is nevertheless misleading when one views the figure (Fig. 8-22), since effect estimates of 4 of the 5 the cities with the most power are very small, and obviously not significant. The characterization of effects of cities with the most

power in the “upper mid-west” and the southeast as tending “to be positive and not far off the nationwide mean” (p.8-246, L18-19) is also misleading, since for the “upper mid-west”, two of the top 3 show either no effect or are negative, whereas for the southeast, two of the top 4 are negative (Fig. 8-23, p.8-245).

The issue of heterogeneity is important. I don’t find a clear discussion (I may have missed it) of the fact that a statistical test for homogeneity of effects in the revised NMMAPS failed to reject, prompting the investigators to conclude that there was no statistical evidence for heterogeneity of effect. However, the power of this test to detect heterogeneity is low, given even less precision in the city-specific effect estimates in the revised analyses. The issue of heterogeneity of effect is still therefore a very open question.

The statement that low effect estimates in NMMAPS tended to be seen in cities with lower PM10 concentrations (p.8-246, L26) is also incorrect. In fact, the opposite is true. When the NMMAPS investigators explored city-level factors that might relate to PM effect estimates, mean PM concentration tended to be negatively associated with the PM effect estimate, indicating that cities with lower PM concentrations had higher estimates of PM effect, and vice versa.

11. Measurement error.

The discussion of the role of measurement error (p.8-250, etc.) is generally well done, and emphasizes the important distinction between total personal PM and personal PM of ambient origin. The issue as to whether measurement error can account for the potentially falsely negative estimates of coarse PM effect is not well resolved in the CD. The findings of Carrothers and Evans (p.8-253, L1) tend to question this assumption. A statement should be made either that this is still an open question, or that the general assumption regarding the impact of measurement error on effect estimates still holds.

Section 8.4.8.4 (beginning p.8-264) largely describes the measures of PM exposure used in the several cohort studies. As opposed to the preceding section on measurement error in the time series studies, there is little attempt to interpret the role of measurement error in impacting estimates of effect in the cohort studies.

Specific &/or editorial comments.

8-5, L17: Prospective cohort studies should be distinguished from panel studies, since these are qualitatively much different.

8-8, L22: The sentence itself is merely confusing, but the phrase in parentheses is the correct criterion.

8-10 to 8-12. This discussion of effect modification is very confusing and would not enlighten anyone not already familiar with the concept. I was unable to figure out what the example was attempting to demonstrate. Although co-pollutants could be effect modifiers, the use of the figure in this context makes the concept opaque. I recommend using a clearer example.

8-12, L21: A change in effect estimate (without a change in standard error) is sufficient to suggest confounding. Leave out the reference to standard error in this context.

8-16, L25: The 1.4% estimate is based on strict GAMs, not on GLM, for which case the estimate was 1.1%.

8-27: In the comments in the table on Gamble, how can NO₂ be both associated and not associated with mortality?

8-64, L16: While this general statement is true, how is it particularly relevant here?

8-73, L31: The Goldberg study did not investigate deaths due to CHF. They looked at total non-accidental mortality in the stratum of patients with pre-existing CHF. This needs clarification.

8-104: The last AHSMOG superscript should also be “9”.

8-111, L28: This sentence is confusing. Are you suggesting that confounding factors should not be included in a model, and that the effect estimates from other cohort studies not including these confounders are not confounded?

8-157, L4: This sentence suggests that the evidence is good that acidic particles are more toxic than less acidic particles. That assertion is not true.

8-159, L9: Reporting the joint effect of PM and carbon monoxide is an interesting approach to avoiding the finding in this study that the effect of carbon monoxide was stronger than that of PM, a somewhat puzzling finding unless one acknowledges the role of gaseous pollutants as surrogate measures of something.

8-165, L18: “...cardiac respiratory disease...”? Should this be, “...cardiorespiratory...”?

8-169, L6: “had were”?

8-186, L18: The value of cross-sectional studies consists in the very fact that there is person-to-person variability. The difficulty is that because of this large variability, there may be so much noise that one cannot observe the exposure-effect signal.

8-190, L22: I would dispute the statement, “Substantial prior knowledge to guide model fitting now exists ...” This supposed “prior knowledge” is itself largely based on models driven by data, not on extant knowledge, an example of circular reasoning.

8-191, L13: The depiction of the confidence interval or p-value as indicating anything about whether a finding is “real” or due to statistical artifact, is incorrect. Assuming that the model is correctly specified, and that there is no confounding, the p-value tells us how likely it is that the finding could be observed by chance. The last sentence of that paragraph is getting at the more important issue of model specification.

8-193, L22: Although this statement is strictly true, it can be confusing. Since the estimates of effect themselves were typically around 1 to 2%, it is true that most revised estimates did not indicate an absolute reduction of 1%. However, percentage reductions in the effect estimates themselves were sometimes very large, some greater than 50%.

8-196, L21: Should this be “larger” risk estimates, rather than “smaller”?

8-197, L25: The fact that the 95% confidence intervals overlap is not necessarily relevant to the assertion that the effect estimates from the two models are not statistically different. See van Belle G (2002). Statistical Rules of Thumb. Wiley, New York (p.39).

8-202, L18: Drop “an.”

8-217, L16: In Hong Kong, I would agree that the decrease in SO₂ was “substantial”. However, I would not agree that the decrease in sulfate was “appreciable”: I would think “trivial” was more appropriate.

8-221, L4: Should not the Lippmann/Ito work from Detroit be included in this section?

8-247, L19: HEL should be HEI.

8-268, L5: Should be Table 8-40, not 8-38.

Chapter 9 (Integrative Synthesis)

1. General.

A better job could be done to integrate important points across the various chapters of the CD in order to present a compelling picture of the recent progress that has been made in understanding PM health effects. This is a missed opportunity. For example, the more recent toxicologic and human experimental data have provided some added credibility to the epidemiologic data that would not have occurred in isolation. Although there are some attempts

to present this perspective (p.9-51 & 9-132, for example), the effort to fully summarize the CD as a whole I believe gets in the way of a more informative synthesis.

There is more objectivity and appropriate caution in many summarizing and concluding sections of this version, for example in noting individual-city differences (p.9-84, 1st para), noting that age differences in cardiovascular admissions are “neither striking nor consistent” (p.9-104, L3), and noting that PM effects and gaseous pollutant effects have varying degrees of robustness (p.9-112, L27). However, perhaps too strong, for example, is a statement such as the following (p.9-112, L1): “The evidence from recent time series studies of CVD admissions suggests rather strongly that PM effects are likely maximal at lag 0, with some carryover to lag 1.”

2. PM as a surrogate measure.

A reasonably good job is done in presenting a balanced view of the role of a PM metric in epidemiologic models (p.9-67, L10; p.9-69, L14, etc.) as potentially that of a surrogate measure. I would have gone even further and added that the PM metrics, given that they are exquisitely sensitive to meteorology, also likely incorporate some poorly captured aspects of meteorology in addition to just some features of the general air pollution mix.

3. Gases as surrogates.

I have discussed this issue in my comments to chapter 8 (point #2). In short, this approach (section 9.5.4 [p.9-33 to 38] & p.9-116, L3-10) to attempting to undermine the role of the gases as legitimate confounding factors in time-series studies fails once it is understood that gases likely serve as surrogate measures of otherwise poorly-measured, time-varying confounders. It is unlikely that gases merely serve as measures of features of PM; PM itself likely serves to some extent as a surrogate measure.

4. Sensitivities.

In general, there is expressed awareness of the sensitivities of the observational estimates of effect to modeling issues. I disagree, however, with the statement, “The ecologic time-series morbidity studies generally have controlled adequately for weather influences” (p.9-105, L1). See point #6 in my comments on chapter 8.

5. Coarse PM.

Good summary. The postulated effects due to coarse PM in one place are argued to be due to “biogenic materials” (p.9-85, L29), and in another place to metals (p.9-90, L10). This is confusing. Presumably the effects of fine PM are also likely a function of composition, so this should not be used as a tack to attempt to “explain away” the coarse PM findings.

6. Utah intervention study.

The Utah story (p.9-128, L12, etc) is complicated. The decrease in monthly hospitalizations associated with closure of the steel mill was seen in association with marked reductions in PM concentrations, which alone could have been responsible for the health benefit. It has subsequently been learned that, not surprisingly, particle composition and toxicity from mill emissions differ from those of non-mill ambient PM. So, both composition and concentration changed during the mill closure, and we have little insight into which change was the critical change, or whether both were important.

Also regarding the Utah toxicity studies, is it really credible that instilled delivery was comparable to that experienced by the exposed population (p.9-128, L17, etc.)?

As noted in my comments to chapter 8 (point #8), the only outcome studied relative to the closing of the steel mill was monthly hospitalizations; mortality was not an outcome (p.9-58, L20), having only been studied through a traditional time series design of daily mortality in that setting. Note that the reference should have been to Pope et al., 1992, not 1999b, but that is now moot, since the reference to mortality is no longer relevant.

7. Range of estimated effects.

In focusing on ranges of effects (p.9-127, L22), why use the mortality range of 2.5% and above for a 50mcg/m³ increase in PM₁₀, when the NMMAPS estimate is 1.1%? Similarly, for cardiovascular mortality (L25), the NMMAPS estimate is much lower. Certainly NMMAPS is an outlier, but there is no agreement that it is biased low, and should therefore be retained as the low point of the range. Note, to be consistent the PM₁₀ estimates, even for hospitalizations, should be expressed per 50mcg/m³ increase in PM₁₀.

Specific &/or editorial comments.

9-53, L2: goral = goal.

9-69, L1: Lack of statistical significance does not always, and one would hope rarely, reflect low statistical power. Lack of significance is meant to suggest that an association is not in fact present.

9-108, L5: The reason that reporting the best lag introduces bias is that there is some randomness to the effect estimates across lag. I don't know what point is being made in the second phrase of that sentence.

9-117, L15: I can't make sense of this sentence. Is there a mistake somewhere?

9-118, L10: I would replace “experimental” with “clinical”. L14: I don’t believe that “standard statistical methods” do adequately handle these problems. L19: raise = rise.

9-122, L8: There is an extra “;” here. L12: the Lipfert study was also national in scope.

9-126, L19: ZPM?

9-127, L13: It is not clear why this paragraph is inserted here. It seems out of place in a discussion of lung function and symptoms. L16: These associations are not “strong”. A strong association would be an RR of, say, 2.0 or higher. These are 1.2 at best.

Dr. Barbara Zielinska

Chapter 2 of the 4th External Review Draft of PM CD

Physics, Chemistry, and Measurements of PM

In my opinion this chapter is ready and does not require further CASAC review in this round of PM NAAQS CD. This last version (4th) represents a significant improvement over the previous (3rd) version. The addition of a section discussing the definition of particle diameter (section 2.1.2.1), more thorough discussion of physical properties of particles, and the inclusion of the latest scientific findings, improved the quality of the information contained in this chapter. Also, moving the detailed discussion of measurement and analytical techniques to the appendices greatly improved the clarity of presentation. I don't have any further specific comments regarding this chapter.

Chapter 3 of the 4th External Review Draft of PM CD

Concentrations, Sources and Emissions of Atmospheric Particulate Matter

This Chapter is very close to completion and I have only a few specific comments, as follows:

1. Page 3-76, Table 3-9. This table does not contain the important results from the Northern Front Range Air Quality Study, showing the dominant contribution of gasoline vehicles to ambient PM_{2.5} concentrations (Watson et al., 1998). The two studies that separated diesel and gasoline PM shown in this table are not sufficient to support the statement on page 3-79, line 1-2 that the gasoline vehicles make significant, and sometimes the dominant, contribution to ambient PM_{2.5} concentration.
2. Page 3-93, line 2-10, estimates of emissions of potential precursors to secondary PM. The authors recommend multiplying the emissions of SO₂, NO_x and NH₃ by factors of 1.5, 1.35, and 1.07, respectively to account for their chemical form in the aerosol phase. However, not all gaseous emissions are converted into aerosol form. In addition, the factor of 2 was never suggested by Turpin and Lim (2001) for conversion of VOC precursor to aerosol phase. They suggest this factor for conversion of organic carbon (OC) concentrations into organic compound mass concentrations, for nonurban aerosols only.
3. Page 3-102, line 21: does this mean "experimental data"?
4. References should be updated. Is Bahadori et al, 2000a,b, still in press?

Chapter 5 of the 4th External Review Draft of PM CD

Human Exposure to PM and its Constituents

Although this chapter has been improved over the previous version, it is still difficult to read because of the detailed reviews of individual papers. The CASAC review of the 3rd draft of the CD recommended: “We very strongly suggest that an alternative approach be taken in which the chapters provide the integrated summary of the applicable science highlighting what is known, but that the detailed discussions of individual papers that need to be included and reviewed go into appendices to the document (not to the chapter).”

The organization of Chapter 5 does not follow this suggestion... In addition, the Summary Section (5.6) has not been significantly revised in comparison with the previous version. For example, the statement on page 5-122, line 9, says that PM mass concentrations, especially fine PM, are distributed relatively uniformly in most metropolitan areas. In contrast, Chapter 3 discusses the spatial variability of PM concentrations within a city (see for example page 3-100, line 4-14, and 3-103, line 22).

Dr. Jane Q. Koenig

PM CD
June 2003

Executive summary

Reads well. May need a few adjustments regarding emphasis.

Page E-5. Section 8. Glad to see biomass fuels included

Page 8. Section 2. Remove sentence "No such techniques exist for coarse particles" The doc includes data for PM10-2.5 so this sentence is incorrect.

Page 9 first sentence. concentrations **in** many urban (in was omitted)

Page 10 Section 13. 2nd sentence. its should be **their**--to agree with the antecedent.

Page 16. I like the conclusion regarding acid aerosols.

Page 18. Is there really STRONG evidence from CAPs studies regarding chemical composition???

Page 19. Section 2 line 8 **airway** is one word. Section 4 first sentence **fed** not led

Page 20 top of page. This paragraph gives the impression that non-diesel PM has no effect on asthma? I don't think we want to make that assertion and recommend that a more thorough summary of asthma effects be included here.

Page 22. First complete line. The l has been deleted from Model

Page 23. Section 4. I don't think PM should be used in a possessive sense.

Pge 24. Continuation paragraph. Don't leave the reader with the impression that wood smoke particles are mainly coarse as they are mainly fine (, 1 micron). What are the coarse particles from wood burning??

Page 25. Section 10 I would include mention of CF and mortality in this section.

Section 11. I think this section would be strengthened by inclusion of data. Percentage increases are given for mortality. Same should be the case for morbidity.

Page missing!!!

Page 28. Section 4. The Dublin study should be included here as another example of an

intervention study. Also Atlanta Olympic games included PM data.

Section 7. I object to asthma being described as not a serious disease. It is the most common chronic disease of childhood, the main cause of school absences, and the health care costs annually in the US are \$14 billion.

Page 43. Section 17. I think there should not be such emphasis on metals. The epidemiologic data don't justify this.

Chapter 9. Integrative synthesis

(I concentrated on the health portions of this Ch)

9.7.2.1

p 56. Line 21-23. Have the effects with MgO and sparked carbon been replicated. If they are single observations we need to be careful in the description of results.

9.2.2.2

Line 13. I didn't think the controlled lab studies were conducted at H₂SO₄ levels that were distinctly higher than ambient. I thought peak values at 100 ug/m³ had been reported.

9.7.2.3

page 9-61. It might be good to list the properties of particles associated with tox effects.

9.7.3.

line 14, I think HRV and markers of thrombosis and coagulation need to be added here. They are discussed in this section.

9-63

line 5. Why would one consider that one observation is a single event. There may be similar events whenever the same conditions are present. Just because HTV isn't being recorded does not imply it is not occurring!!

9.8.1

page 9-66; line 22 cardiac illness needs to be added to this list. This section must be a carry over from a much earlier version.

Table 9-8 is good, easy to read. However for Mar the PM size info has been left out.

Page 9-84, line 27. Should be Table 9-8.

Conclusions regarding PM-CVD morbidity

Page 9-104

Temporal pattern. We really need to look at more lag times (hourly) using the continuous monitors.

Susceptible populations. Diabetes has not been mentioned at all in this chapter (unless I missed it). The addition of diabetes as a group susceptible to effects of PM needs to be integrated into the chapter. Same with pre-term births and other reproductive effects. This later was an item that CASAC asked EPA to include in this draft and it is barely mentioned..

Section 9.8.3 reads well. I think this is a useful summary. However I wonder whether section 9.9 should precede it rather than follow it. It seems we should discuss susceptible populations prior to discussed health data from those populations.

Page 9-122

References in Table. G is missing; H is used twice

Line 5. Its Pope et al. 2002. This is correct elsewhere in this section

Page 9 126. In this paragraph I think reference to Table 9-11 would be useful.

Page 130 Line 3. So far, the only mention of reproductive effects.

Chapter 8.

This chapter is very similar to the previous draft. Where changes have been made they are generally good. Some tables have better formatting in my opinion.

8-118 8.3.1

somewhere in this section, there should be a discussion of diabetes as a risk factor for hospitalization with cardiac disease.

Some areas of concern. Page 8-146; 8.3.1.4.

I suggest including panel study results summary in this section. It appears to be restricted to hospital admissions. What have we learned about susceptible populations from panel studies?

Minor point line 8 data are

I think a point can be made that the results of CV effects in panel studies support the epidemiology.

Page 8-147

Under temporal patterns. Mention the 2 hour lag with the MI study in Boston. We should make the point that more short term (1-4 hr lag) studies should be conducted now that continuous PM data are available.

In terms of chemical composition, are there any published data on composition from panel studies?

Page 8 -154

This last paragraph the respiratory hospital admissions section summarized two intervention studies. Should intervention studies have their own section to emphasize their importance? Why isn't the Clancey study in Dublin mentioned? I note that no citation to it is in the references.

In fact, I recommend that this coverage of intervention studies be merged with section 8.4.3.4. There is duplicate material between the 2 discussions.

8-206 and following

Good new discussions of issues.

8.4.3.4 Page 8-213

This is a new section and very useful. I believe these data will be directly useful in standard setting agenda. Should include the Dublin study.

8.4.4.

page 8-219

I am confused. I thought data on PM components and mortality had been presented earlier.

Why is it brought up again? If it is for interpretative use, should it be in Ch 9? 8-222 Mar, Tsai, and Laden have been described earlier.

8-224. Cardiorespiratory mortality has been covered.

The section on lung cancer appears new (and useful).

8-4.4.2 fine v coarse morbidity. I think this belongs in 8.3. Morbidity effects of PM exposure

8.4.4 the section on lags is good as are the following sections. However, as I said in my review last year, I think these sections should be shortened and that conclusions belong in Ch 9 (or the staff paper).

Removing figure 8-24 is good!

8-5 Summary

In general I agree with the summary.

#7. I repeat that I think there should be a mention of diabetes as a risk factor for PM-induced cardiovascular effects.

Regarding epidemiology, under # 17 I recommend describing these new effects relating to infants or very young children. There is a wealth of data on PM effects in children. It is the reproductive data that are new.

This concludes my remarks. Please contact me for clarification if needed! Thanks Jane

Dr. Petros Koutrakis

Below please find my review of Chapter 5 “Exposure Assessment”:

General Comments:

I would like to applaud the authors for the wonderful job they have done. The exposure chapter is very comprehensive and includes many relevant results from recent exposure studies. Although the chapter is somewhat verbose and pedagogic, causing distraction from the main points, it is still likely that many new researchers in the field will benefit from reading it. While it might be better if this chapter was reduced by about 20% (without losing its content), it is probably not worth the trouble at this point.

The authors have included an important section on the relevancy of exposure assessment to epidemiology and toxicology. I agree with most of its conclusions. However, it needs to be concise and better focused. It contains a great deal of basic material which was already reported earlier in the chapter. As a result, the important issues are obscured and disconnected. Considering the importance of this section, I would suggest that an effort be made to clean it up.

Furthermore, the chapter talks a lot about the variability of the infiltration ratio of ambient particles. Also, there is some discussion about acute versus chronic exposure assessment. The message that ambient concentrations can be appropriate surrogates of personal exposures to ambient particles for acute epidemiological studies is clear and correct. In contrast, the message that ambient concentrations may not be an accurate exposure metric for cross-sectional epidemiological studies is not clear at all. It is nice that the comprehensive discussion that is presented suggests that the impact of ambient concentrations on the indoor environments can vary by season and geography. However, the implication of this conclusion is not obvious. Findings from the recent exposure studies suggest that for an ambient concentration of 10 micrograms per cubic meter in Boston, Atlanta and Los Angeles the resulting population exposures to particles of ambient origin will be very different. This can be of paramount importance in our efforts to investigate the chronic effects of particle exposures. I am sure that the authors would agree with me. So even though it is possible that novice readers would reach this conclusion on their own, it should be stated explicitly to make sure that this important message is not overlooked.

Specific Comments:

Section 5.2.4.1.1: Since the authors provide references for personal continuous monitors, they should do the same for personal integrated samplers. Also, something should be said about the accuracy of the continuous monitors. I think it is always necessary to do some personal sampling with both integrated and continuous methods for calibration/QA-QC purposes.

Figure 5-2 and related discussion: There is a nice discussion about the impact of outdoor sources to indoor concentrations or personal exposures. The comparisons between the impact fractions for indoor concentrations and personal exposures are very elucidating. There is also a discussion about

the use of sulfate as a tracer of outdoor sources. My recent experience suggests that the regression and sulfate methods do not agree as well as we would like, and that the impact fractions are lower when calculated using the regression approach. We have found that this discrepancy becomes more pronounced when correlations between outdoor and indoor concentrations become weak, e.g. poorly ventilated homes. It is conceivable that, for the weaker indoor/outdoor associations, the regression slope is biased downwards as one might expect. This is a new piece of information and we need to work more on this analysis. My point here is that it may be worth it to discuss the two methods more critically than is possible in the criteria document.

Page 5-54: I am not sure that the comparison of indoor/outdoor ratios from the Fresno and Baltimore studies is very meaningful. As we know, the composition of particles is not the same for these two locations. In Fresno ammonium nitrate represents a much larger fraction of fine particle mass. Because this compound is in equilibrium with its precursor gases, ammonia and nitric acid, its partitioning between the gaseous and particulate phase can be easily disturbed while outdoor particles are indoors. Thus differences in indoor/outdoor ratios between Fresno and Baltimore could be a function of ventilation, indoor sources, and sampling artifacts.

Page 5-104, line 16: Avoid using “feel” because it is too awkward.

Dr. Allan Legge

August 23, 2003/ September 1, 2003 Additional Comments

TO: Dr. Phil Hopke/ Mr. Fred Butterfield

FROM: Dr. Allan Legge

Review Comments: Fourth External Review Draft of Air Quality Criteria for Particulate Matter (June, 2003).

Chapter 3: Concentrations, Sources, and Emissions of Atmospheric Particulate Matter

Overall Comments:

The text of this Chapter is very well done. The matter of 'background concentrations of PM in the United States', however, is still problematic. The use of annual or longer time period averaging times is questionable. Given the spatial as well as the seasonal variability in natural background PM concentrations, it would seem more appropriate to at least use a seasonally adjusted natural background. The idea that 'policy relevant background' circumvents this issue is difficult to defend. Clearly more work is needed in the future to adequately characterize natural background PM concentrations across the United States especially in terms of PM_{10-2.5}.

One area which needs emphasis in the future relates to the need to characterize PM deposition rates in forested areas of the United States where 'nitrogen saturation' has been identified as an issue in Chapter 4 of the PM CD. There is a need to not only characterize the PM mass but also the chemical composition of the mass that is potentially deposited to these forests. That being said, it is very important to keep in mind that PM represents only a portion of the 'total cumulative load' over time of air pollutants (both wet and dry) to which these forests are exposed. The extent to which PM deposition has played or is playing a role in the 'nitrogen saturation' of forest ecosystems in the United States needs to be determined. This information is needed for the welfare risk assessment for forests as well as for the risk assessment of eutrophication of aquatic ecosystems.

Work needs to be done on the 'references' especially in the Appendices. Many of the papers cited are still listed as 'in press' or 'submitted'. One paper listed as being 'submitted' has a '2004' date on it and is by Lefohn et al. (2004). The EPA policy on what papers can or cannot be included in the CD must be consistent.

Specific Comments:

1. Page 3-85, lines 3-5 and Figure 3-23, lines 1-2.

Reference is made to the "Chilliwack Airport in northwestern Washington State".

The 'Chilliwack Airport' is located in southwestern British Columbia, east of the City of Vancouver along the Frazer River.

2. References

- i) Page 3-105, Bahadori et al. (2000a and 2000b) listed as 'in press'
- ii) Page 3-106, Gillies et al. (2000) listed as 'submitted'
- iii) Page 3-107, Husar et al. (2000) listed as 'submitted'
- iv) Page 3-108, Lefohn et al. (2004) listed as 'submitted' and listed twice.
- v) Page 3-109, Pinto et al. (2000) listed as 'submitted'

3. Appendix 3A

- i) Page 3A-3, reference by Pinto et al. (2003) listed as 'submitted'.
- ii) Page 3A-12, Figure 3A-9, vertical axis in (b) incomplete, should read $PM_{2.5}$ ($\mu g/m^3$)
- iii) Page 3A-14, Figure 3A-11, same as (ii) above.
- iv) Page 3A-17, Figure 3A-17, same as (ii) and (iii) above.
- v) Page 3A-41, Figure 3A-37, 'key' in upper right hand corner lists Site A, Site B and Site C while the 'map' to the left shows only (A) and (B) and (?).

4. Appendix 3B

- i) Page 3B-2, lines 8-10.

This sentence discusses the matter of 'minimum detection limits (MDL)' which is fine. The problem is that in a number of the 'Tables' the 'minimum' (min) level detected is lower than the reported MDL. This needs to be corrected or clearly explained why this is the case.

5. Appendix 3D

- i) Page 3D-1, line 15, and page 3D-23, line 22 and 25.

The reference 'Warneck, 1988' is used. While this is fine, the Second Edition of this book was published in 2000 and would be more appropriate.

6. Appendix 3E

- i) Page 3E-1, lines 20-21 and page 3E-5 lines 30-31.

The reference 'Lefohn et al. (2004)' is listed as 'submitted'.

Chapter 4: Environmental Effects of Airborne Particulate Matter

Overall Comments:

This Chapter reflects a substantial improvement over that presented in the Third Draft of the PM CD especially in terms of the logical flow of the text. The use of the EPEC Framework, in this regard, is helpful to the reader. That being said, the details of the EPEC Framework are rather cumbersome to apply in a clear and concise manner for air pollutants. It is clear from the text that PM, especially in the form of nitrogen, is having an adverse effect on some forest ecosystems in the US and is seen as 'nitrogen saturation' as well as eutrophication in some aquatic ecosystems. These 'adverse effects' have resulted from chronic long-term exposure of

these ecosystems to N deposition. Put another way, it is the ‘cumulative load’ of N which has resulted from the chronic long-term exposure of these ecosystems to N deposition which is the problem. The problem is made worse by the fact that these ecosystems also have a history of exposure to other air pollutants (i.e. multiple stresses). The European concept and approach of using ‘critical loads’ to protect ecosystems has great merit and needs to be seriously considered for PM. The current US approach for air quality standard setting does not adequately address the issue of the ‘cumulative effects of air pollutants’ on the environment. A major paradigm shift in thinking is required and is strongly recommended to ensure the long-term sustainability and protection of the environment.

Specific Comments:

1. Page 4-6, line 27 -28.

Suggest this read “- - -, having been emitted from area, point or line sources as fully formed particles - - -“

2. Page 4-7, line 10 plus additional pages and lines as listed.

It is stated that “HNO₃ has an extremely high deposition velocity, nearly independent of the physiology of the surface.” It is unclear what is meant by the “physiology of the surface”. This same concept occurs on the following pages as well:

On page 4-9, line 4, reference is made to “the physiological activity of the surface”.

On page 4-28, line 2, reference is made to “physiological characteristics of the surface”. On page 4-39, line 31, reference is made “to surface physiological properties”.

On page 4-61, lines 7-8, reference is made to “the physiological activity of the surface”.

3. Page 4-8, lines 8-9.

It is noted that “- - - direct injury due to SO₂ is commonly observed near uncontrolled point sources.” While this is true, the statement implies that direct injury to vegetation from SO₂ is only observed near uncontrolled point sources. Direct injury to vegetation has been observed near SO₂ point sources where SO₂ emissions controls do exist.

4. Page 4-21, lines 30-31 and page 4-22, line 1.

It is noted that “Collection and analysis of stem flow and throughfall provides useful estimates of particulate deposition when compared to directly sampled precipitation.” While this is true to a point, there are some large uncertainties in these data. A very recent field intercomparison of throughfall measurements paper by Bleeker et al. (2003) is very helpful regarding the uncertainties of throughfall and stemflow measurements.

Bleeker, A., Draaijers, G., Van der Veen, D., Erisman, J. W., Möls, H., Fonteijn, P. and Geusebroek 2003.

Field intercomparison of throughfall measurements performed within the framework of the Pan European intensive monitoring program of the EU/ICP Forest.

Environmental Pollution 125: 123-138.

5. Page 4-23, line 17 and page 4-29, line 15.

Reference is made to “coarse PM₁₀”. What is meant here? It should be consistent with Chapter 2.

6. Page 4-24, line 24 and page 4-36, line 28.

It is noted that V_d for SO_4^{-2} is approximately $0.16 \pm 0.08 \text{ cm}^{-1}$ on page 4-24 and that the mean daily V_d for sulfur-containing PM to be 0.6 cm s^{-1} on page 4-36. How can this be the case?

7. Page 4-28, line 19.

Suggest this read “tend to be the cleanest, with most particles accumulating in the midvein central portion of the leaf.”

8. Page 4-49, line 15.

What is “atmospheric meteorology”?

9. Page 4-50, line 30.

Should read “the Hubbard Brook Experimental Forest (HBEF)”.

10. Page 4-71, lines 14-26.

The following statement is made. “However, current levels of sulfate deposition reportedly exceed the capacity of most vegetative canopies to immobilize the sulfur (Johnson, 1984).” The Johnson, 1984 reference is rather old to imply that current (i.e 2003) sulfate deposition is exceeding the capacity of most vegetative canopies to immobilize the sulfur.

11. Page 4-88, line 14.

Suggest this read “pathway of PCDD/Fs compared to aerial plants parts.”

12. Page 4-95 to 4-98, Effects of Nitrogen Deposition

A number of references cited in the text are missing from the ‘References’ section. Examples of missing references are as follows:

Galloway and Cowling, 2002

Rabelais, 2002

van Edmond et al., 2002

Aber et al., 1995

Howarth et al., 2002

13. Page 4-96, line 13.

What is “regional and global (2002: Galloway and Cowling, 2002 - -).” There is either a reference missing or “2002:” is a typo.

14. Page 4-96, line 16.

Should read “humans and ecosystems (Rabelais, 2002; - - -”.

15. Page 4-100, line 5.

Should read “(6-11 kg ha⁻¹ y⁻¹ as throughfall)”.

16. Page 4-102, Table 4-14, Footnote a) line 2, and Footnote d) line 1.

Reference is made to the “wet deposition/ total N deposition ratio (0.56)” in footnote a) and the “throughfall/total N deposition ratio (0.56)” in footnote d). The first point is how can these ratios have the same value when the numerator in one is wet deposition and the other is throughfall. Further, in footnote d) ratio is misspelled ‘ration’.

17. Page 110, line 21.

Should read “- - - -. Nitrogen concentrations were high in mature ecosystems after”

18. Page 125, line 1.

Should read “region. Time scales of response - - - “

19. Page 4-148, line 3.

The generic name “*Rhododendron*” should be in italics.

20. Page 4-149, lines 10-11.

Suggest that the following sentence be deleted: “Their influence on the environment has been pervasive for thousands of years.”

21. Page 4-151, line 20.

Should read “ site of heavy metal - - - - and provides both a habitat and a resource”

22. Page 4-193, line 22.

Close up space between sentences.

23. Page 2-227, line 25.

Should read “ and indicates the status - - - - -“

24. Page 4-230, line 7.

Should this read “ - - and exceeds critical loads; - - “ rather than “ - - and exceeds critical thresholds; - - “

25. Page 4-232, line 4.

Should read “hydrogen ion in acidic precipitation, - - - “

26. Page 4-233, lines 14-16.

The end of this sentence is incomplete.

27. Page 4-234, lines 8-9.

It is stated that “Ecosystem effects have been observed only in the neighborhood limestone quarries.” It would be more accurate to say that “Ecosystem effects have been observed in the neighborhood of limestone quarries.” There are effects on vegetation near heavy metal smelters where both PM and SO₂ are present. It is a ‘mixture’ issue in this case.

Dr. Paul J. Liroy

Paul J. Liroy, Ph.D. Professor, Environmental & Community Medicine, UMDNJ-RWJMS, and Deputy Director Government Relations Environment and Occupational Health Sciences Institute

Review: Chapter 3 AQCD: Concentrations, Sources and Emissions of Atmospheric Particulate Matter.

General: A very good summarization of a very large and disparate data set. I still have some issues with the method of presentation of data, and they will be addressed in my comments below.

Specific Comments:

1. Figures 3-1a, 3-1b, 3-4a, and 3-4b. I still do not understand the reasons for the designated concentration ranges, why $0 < x \leq 23$, $23 < x \leq 38$, and $x \leq 38$ (For Annual). These make no sense. You should consider $0 < x \leq 25$, $25 < x \leq 50$, $x \leq 50$. The current designations on each table should have at least one benchmark being the current standard.

Please, consider for PM_{2.5} : Annual $0 < x \leq 7.5$, $7.5 < x \leq 15$, $x > 15$;

Highest 98th percentile (daily): $0 < x \leq 33$, $33 < x \leq 65$, $x > 65$.

2. P 3.16 and 17. 3.17 a., b., and 3. c., d. respectively: See Appendix for rest of plots. The range for the Y Axis is not the same in each case. These are “mindless” computer plots. You should have a standardized Y Axis for the 24 hour average PM, e.g. 0-110 : g/m³. Otherwise, it is difficult to compare the range of values in each plot area. There are a large number of charts, and the document should make it easy to visually compare results. This problem exists throughout the document and the appendices.

P 3.25, lines 5-13, and through P 3.30, line 5: The presentation of the frequency distribution for the early 1990’s is fine, but you should also compare the results from the same cities using the more recent data in the Appendix A from 1999 through 2001, e.g. 3A-29, Riverside; 3A-4, Philadelphia.

P 3.74, lines 17-18: Very good point.

P 3.74, lines 19-28: In the past, investigations have also used cooling and heating degree days.

P 3.75 – 3.79: I think there needs to be a bit more frankness about the fact that these models cannot accurately apportion the sources of SO₄-2 and NO₃-1. This is an important concern since each can be a major constituent of the aerosol. I am very please with the progress on molecular markers for source of organic particles. However, again this continues to be important research needed to help the states develop appropriate State Implementation Plans.

P 3.83, lines 4-14: Example of general concern: Research on long range transport of dust has been published long before 1991. The important contribution to the current document is the quantification of the amounts, which should be stated in this paragraph as an objective.

P 3.89-91: This discussion on PRB should have two distinct sections: Western Aerosol and Eastern Aerosol, with conclusions presented for each region. It will help the reader.

P 3.93, Table 3-11, P3.94, Table 3-12: Could this be sub-categorized for percentages according to West and East emission sources? Some will have higher percentages in East, others will have higher percentages in West.

P 3.99, lines 24-31: Somewhere in the summary there should be an indication of the percentages of sites above annual standard (West/East) and the frequency of violations of the 24 hour standard (West/East).

P 3.104, #3: PRB. The case for the ranges needs to be more clearly stated in the text.

Review: Chapter 5 AQCD for PM: Human Exposure to Particulate Matter and its Constituents

General: The June, 2003 version of chapter 5 is a much improved document. I commend the agency and the authors in their efforts to bring the advances and concerns about exposure to PM into focus. I do have a few addressable concerns, and they are discussed below.

P 5.1, line 22: Replace "Exposure has many definitions" with "Exposure to environmental contaminants can be interpreted in a number of ways."

P 5.2, Table 5-1: An excellent comprehensive presentation of the variables required to categorize PM exposure.

P5.8, line 2: Need references, two that are already in the document are Lioy (1990), NRC (1991).

P5.8, lines 21-23: Well stated point.

P5.13, lines 8-13: Based on the fact that we still are not sure about the absolute timing of an adverse PM event, short time samples may be better for explaining acute effects (cardiac or asthmatic events). The point: shorter sampling times may not increase errors, may reduce errors.

P5-25, line 2: Sulfate would have a size distribution within PM_{2.5}, not necessarily a distribution that is the same size distribution as PM_{2.5}. SO₄-2 would more strongly mimic the sub-micron fraction of the fine particle fraction that penetrates into buildings.

P5-6, line 20: Add a reference from current list, NRC (1991).

P5-31, lines 7-10: Drop sentence. Not relevant to AQCD.

P 5-52 lines 9-10: Are four significant digits justified?

P5-55, line 2: What does “excellent” mean in this sentence? Do you mean “high”?

P5-78, lines 24-28: In cases of summertime smog O₃ and PM_{2.5} can vary together. Therefore, the resulting products of reactions between O₃ and other precursors may correlate with outdoor mass. I think the statement is too emphatic. There is still more research that needs to be done, before the mass is considered non-ambient.

P5-92, line 13: “similar” not “similarly”.

P5-97 line 6: total “particulate” should be total “particle”.

P5-103, lines 13-14: Are you saying that there is a strong correlation between indoor and outdoor concentrations of “acid sulfate”? Please provide references, because in high indoor situations with ammonia, the levels will go down.

P 5-108 and 5-109(through line 11): A good discussion. However, there needs to be a statement that if indoor air is “toxic” it could raise the “health stressor” baseline in a community affected by outdoor air exposure and its health effects.

P5-109, lines 27-31 and P5-110, lines 1-3: A very good discussion.

Key Findings: Clearly presented. The last point should, however, also indicate the need to move from use of ambient levels to the use of ambient related exposures in epidemiological studies.

Chapter 8: PM Criteria document: Epidemiology and Human Health Effects Associated with Ambient Particulate Matter

General: Very comprehensive summary of a difficult topic. I have some concerns that are listed below. My biggest difficulty is finding a way to easily compare results presented from many different studies. It may not be possible to place all in the same format, but the percent increase in mortality or morbidity seem to be the most reasonable. In addition, sometimes the reader is left to guess as to whether or not it’s an increase in daily or annual mortality/morbidity.

Finally, there should be a summary table that lists the RR or percentage changes/x : g/m³ by years of study in those cities where there have been repeat analyses. The point would be to see if things have changed, e.g. has the characters of the aerosol changed since the introduction of PM or precursor emission control programs; and has that led to increasing or decreasing or the same RR/: g/m³?

P 8.10-11: A very good section. Fully supports figures 8.1a and 8.1b.

P 8.17: For the reader, you need to state that the all results and re-analyses will be compared later in the chapter (discussion).

P 8.22, line 13: Need to state how much lower.

P 8.33, line 7: How much lower?

P 8.37, lines 1-18: I am puzzled, this is a 90 city study, and the change is being only considered to be caused by “adjustments in weather”, and not a “reduction in potential risk”. Please explain.

P 8.61, lines 12-23: I am a bit confused, SO₄-2 oxidizes easily to H₂SO₄ ; therefore, it should be a significant part of the local PM Air Pollution. The magnitude of these changes in SOs should; have some influence on health; if, in fact, SO₄-2 is associated with PM health effects. Please clarify or better explain this paragraph.

P 8.63: Lippmann hypothesized H⁺ as marker for health effects in the mid-**1980’s**.

P 8-67, Table 8.4: A major observation from the table is that mobile sources are a consistent contributor to excess mortality.

P 8.75, lines 25-30: You make a point about the multi-city being consistent with the 1996 document, but ignore the fact that the Dominici, et al, analyses yield about 30-40% lower relative risks. Please provide a balanced discussion.

P 8.85: The point about decline in risk with decline in pollutants is important - not just expected. The reason, important “contributing” sources were removed. If RR went up after controls were implemented, it would have meant the wrong sources were being removed. This point needs to be highlighted in the major observations section of this document.

P 8.90, Table 8.7: This table is very confusing. I may be missing something? The table suggests that the mean Risk (last column) is higher than the risks observed for either period used to determine the mean (the results in the first two columns). As presented the results do not seem plausible. In addition, the results seem to suggest, the opposite of the conclusion in the Six Cities Study. After pollution control the RR increases!! This table needs some explanation.

P 8.103: Use of the peak O₃ or the 8 hour average O₃ is much more logical than the mean O₃. Ozone is seasonal, and it impacts on human to health during the times of the day: 10 am and 9 p.m.

P 8-104, Table 8-11: Very well designed table.

P 8-108, Table 8-13: What does Range = 19.9 : g/m³ mean? One number usually does not

represent a range.

P 8-120 – 121: I would limit Table 8-16 to only those studies that did not use GAM or did not use GAM Defaults. The rest could be placed in the Appendix. The discussion should only focus on the non-GAM Default Studies. Thus, the references to studies that used GAM Default should be removed from this section of the document. It confuses the discussion.

P 8-189, line 12: Note: Speciation samples still measure indicators, SO₄-2, etc. But these are much better than just using “mass”.

P 8-193, line 26: The range of corrections go from 0% to 33 reduction in RR for GAM Default vs. GAM without restriction. Further, the largest reductions were found in two largest U.S. studies. Thus, I think the statement on line 26 should be reconsidered and revised to reflect the nature of the results.

P 8-207, lines 11-23: Outdoor O₃ penetrating indoors can lead to production of new secondary particles indoors from indoor precursors thus, a fresh indoor particle with an outdoor contribution.

Section 8.5: Why has the GAM issue been ignored in this section of the document? It was a major issue and the impact (+) and (-) should be discussed as part of key findings.

Dr. Morton Lippmann

Chapter 5 of the 4th External Review Draft of PM CD

Human Exposure to PM and its Constituents

General Comments

This chapter provides a thorough and balanced discussion of the human exposure issues relevant to the review of the adequacy of PM NAAQS. It also makes numerous (and appropriate) references to related literature and discussions in other chapters, highlighting relevant exposure measures used in epidemiological studies.

It is a bit pedantic and repetitious, but serves its intended purpose quite well. It does not need further CASAC review in this round of PM NAAQS measurement.

Specific Comments

p. 5-1, l. 16: Does “emphasis” pertain to this chapter? If not, to what does it pertain?

p. 5-1, l. 25: insert “to PM of outdoor origin” after “exposure”

p. 5-1, l. 26: insert “personal” before “exposure”

p. 5-6, l. 2: change “which” to “that”

p. 5-6, l. 4: insert “inhalable” before “PM”

p. 5-6, l. 24: change “compounds” to “components”

p. 5-7, Table 5-1: for the “General Definitions” column for “C”, add “, except for ultrafine particles, which are generally expressed as number concentrations” after “units” on line 3

p. 5-8, l. 3: insert “generally” before “not”

p. 5-8, l. 6: insert “often” before “not”

p. 5-8, l. 7: insert “most” before appropriate”

p. 5-8, l. 18: insert “that is” after “PM”

p. 5-8, l. 22: change “health effects which” to “some health effects that”

p. 5-9, l. 4: change “unperturbed” to “not significantly affected”

- p. 5-10, l. 11: change “3” to “more”
- p. 5-10, l. 19: insert “mass or” before “chemical” and “constituent” before “concentration”
- p. 5-11, l. 3: change “ambient PM” to “PM of ambient origin”
- p. 5-12, l. 29: insert “time-averaged” before “sum”
- p. 5-43, l. 6: change “determine” to “determined”
- p. 5-67, l. 13: change “Philadelphia” to “Detroit”
- p. 5-67, l. 18: “Lippmann” is misspelled.
- p. 5-75, Figure 5-10: The order of magnitude discrepancy in decay rate for $dp < 1 \text{ : m}$ between the results of Abt et al. and Long et al. is not discussed in the text, and should be.
- p. 5-77, l. 28: What “different properties”? The text should elaborate on the nature of these differences and their implications.
- p. 5-85, l. 22: The text needs to explain the distinction between “resuspended indoor dust” that is “15% from indoor soil” from that is “30% from resuspended indoor soil”.
- p. 5-87, l. 14: insert “of” before “ambient”
- p. 5-92, l. 16: Some readers may wonder what “PM₅₀” refers to. It was not previously defined.
- p. 5-103, l. 6: change “is limited” to “are few”
- p. 5-103, l. 9: change “little” to “few”
- p. 5-113, l. 1: change “particulate” to “coarse PM”
- p. 5-113, l. 27: change “conclusions” to “conclusion”

Chapter 6 of the 4th External Review Draft of the PM CD

Dosimetry of Particulate Matter

General Comments

This chapter is a comprehensive review of the literature on particle deposition, clearance and retention, based on current knowledge. More importantly, it also highlights knowledge gaps, and provides a suitable perspective with respect to considerations elsewhere in the CD on the human health effects associated with exposure to ambient air particles.

The presentations are straightforward, well illustrated, and present an unbiased description that serves the reader well. If the reader is confused, and certainly some readers will be, it is due, at least in part, to the inherent complexity of the subject and the many gaps in the literature.

My major criticism and suggestion for change, other than some specific issues raised below, is that Section 6.6 on Modeling of Respiratory Tract Deposition is fairly repetitious with respect to the literature reviewed in early sections of the chapter. It also is deficient in that it fails to adequately convey that many of the model outputs need to be taken on faith, i.e., need validation by experimental data.

Specific Comments

- p. 6-3, line 20: insert “for some applications” after “useful”.
- p. 6-25, line 6: insert “generally” after “females”, and make “size” plural.
- p. 6-25, line 23: make “ventilation” and “rate” plural and change “was” to “were”.
- p. 6-29, line 7: insert “by ET airway deposition” after “degree”.
- p. 6-29, line 19: change “particle” to “PM surface”.
- p. 6-30, line 16: Three percentages doesn’t make sense for two categories.
- p. 6-47, lines 6-8: Are the percentages by mass or number?
- p. 6-50, lines 14-16: The work of Gehr and colleagues suggests that the particles are wetted and drawn down into the “sol” phase! Furthermore, it should be mentioned that the process was particle size-dependent.
- p. 6-52, line 5: “Minute” is not a good word for this purpose.
- p. 6-62, lines 11-21: This discussion is incomplete without mention of other differences in particle distribution between inhalation and instillation in the lung periphery. Specifically, inhalation produces concentrated deposits on the bifurcations of respiratory bronchioles in humans and on alveolar ducts in rodents, much less deposition on the walls of these airways, and virtually none on most of the gas-exchange area. Instillation, on the other hand, spreads the particle suspension over much more of the surface in those paths that it reaches.
- p. 6-64, line 14: change “more” to “fewer”.

Chapter 7 of the 4th External Review Draft of the PM CD

Toxicology of PM in Humans and Laboratory Animals

The organization and topic coverage are substantially improved along the lines suggested by CASAC, and the reasons for the changes made were well articulated in Section 7.1.

(INTRODUCTION).

The selection of PM types to discuss in terms of controlled exposures and their health effects (i.e., ambient PM, diesel PM, complex combustion-related particles, acid aerosols, metallic PM, and ambient bioaerosols) was very appropriate, and the level of detail and interpretive discussion of each was excellent.

The organization and presentation of the available literature and interpretive discussion of cardiovascular and systemic effects *in vivo* studies in Section 7.3, of the studies of *in vitro* PM toxicity and pathophysiology in Section 7.4, of susceptibility to effects of PM exposures in Section 7.5, and of responses to PM and gas pollutant mixtures in Section 7.6 were very appropriate. The manner in which the findings are summarized and integrated in Section 7.7 can serve as a model for future CD chapters on Toxicology. Overall, this chapter is a highly successful contribution to the overall CD.

Chapter 8 of the 4th External Review Draft of the PM CD

Epidemiology of Human Health Effects Associated with Ambient Particulate Matter

General Comments

This chapter, now matured through its third iteration, and benefiting from the availability of additional in-depth analyses in the peer-reviewed literature, such as the HEI revised analyses of many of time-series studies, is now a comprehensive, well-nuanced, and thoughtful analytical summary of a vast and complex literature. The format is good, i.e., for each issue addressed, there is: a concise presentation of the state-of-knowledge summarized in the 1996 PM CD, a presentation of the most relevant new information, often in clear graphical and/or tabular form, some independent analyses of new studies and groups of studies addressing particular issues, and a brief summation of how the new information and their analyses resolve or at least inform that particular issue. It clearly states what is: known; unknown; ambiguous; and deserving of further investigation. It is also notable for its cross-referencing of relevant information in the exposure, dosimetry, and toxicology chapters. In other words, it is the kind of chapter on epidemiology that CASAC has been looking forward to seeing in a CD since its reviews of such documents began in 1981. Subject to some minor revisions suggested by the August 2003 CASAC review, it is time to close on this chapter, and to commend the authors for a job well done.

Specific Comments

p. 8-7, l. 12: change “associations” to “RRs”

p. 8-39, l. 31: insert “thoracic” before “PM”

p. 8-51, l. 30: should Detroit be referred to as a northeastern U.S. city?

p. 8-56, l. 22: delete “non”

p. 8-87, l. 29: change “dof” to “of”

p. 8-202, l. 22: delete “the following”

p. 8-202, l. 23: add at end “that are highlighted in the discussions that follow”

p. 8-218, l. 30: This discussion is incomplete without reference to the Dublin study.
[Clancy L., et al. Effect of air-pollution control on death rates in Dublin, Ireland: An intervention study. Lancet 360:1210-1214 (2002).]

p. 8-266, l. 19: This discussion is inadequate without mention of the fact that most of the measurements made were below the analytical detection limit.

Chapter 9 of the 4th External Review Draft of the PM CD

Integrative Synthesis

General Comments

This chapter, having had few CASAC reviews, and containing alternate versions of the summaries of the preceding chapters, is inadequate as an “integrative synthesis”. A revised version, which thoroughly addresses scientific issues of greatest relevance to the establishment of primary and secondary PM NAAQS is still needed. To the extent that some parts of the current draft may be useful to supplement or replace the summaries of the other chapters, the following specific editorial changes are suggested.

The current draft fails to integrate the findings of the CAPs studies with the epidemiology, or the support of the dosimetry considerations into the particle-size-specific epidemiological studies. The credibility of the epidemiological associations would be greatly enhanced by including such discussions.

Specific Comments

This introductory paragraph should more explicitly address its role in the setting
p. 9-1, line 11:
of the secondary NAAQS for PM. I suggest adding the following after “PM”: “that need to be considered for decision making in regard to a secondary NAAQS for PM.”

insert “in such samplers” after “fraction”.

p. 9-12, line 11:

insert “chemical and” before “photochemical”.

p. 9-17, line 5:

insert “component” before “signatures”.

p. 9-17, line 14:

p. 9-21, lines 21-23: If this sentence is a correct statement, then it needs some elaboration. Is it due to the location of IMPROVE sites in remote areas?

p. 9-45, line 30: “mucociliary” is misspelled.

p. 9-46, line 9: delete “Also”.

The “40 to 50%” being retained applies to a highly artificial means of inhalation,
p. 9-46, line 15:

and the percentage would be much lower under normal breathing patterns. I suggest replacing
“upwards of 40 to 50% of deposited 6-10 : m” with “some”.

add “and respiratory acini” after “tree”.

p. 9-49, line 17:

I suggest changing “health impacts” to “mortality”. For some other health effects,
p. 9-51, line 2:

the evidence for stronger relationships is much less clear.

p. 9-52, Table 9-6: On this and later chapter pages there is reference to “CoH” (coefficient of haze).
In Chapter 8, this measurement unit is referred (more properly) as “CoH”.

p. 9-56, line 6: insert “larger conductive” before “airways”.

insert “number concentration” after “PM”.

p. 9-56, line 15:

p. 9-57, lines 2-15: This paragraph refers only to acute health effects. The chronic effects findings
of Dockery et al. (1996) and Raizenne et al. (1996) from the 24-city study should also be cited here.

“Ottawa” is misspelled, and also on p. 9-64, line 4.

p. 9-63, line 31:

p. 9-68, lines 10-14: This sentence, as written, would be confusing to most readers. I suggest an
insert on line 12 after “effects”, i.e., “in relatively small segments of the population having special
susceptibilities”.

replace “(e.g., O₃, NO₂, SO₂)” with “and vapors (both organic and inorganic)”.

p. 9-69, line 18:

who is the cosponsor with HEI?

p. 9-70, line 19:

p. 9-102, Figure 9-18: The caption needs to define “IHD” (ischemic heart disease”).

change “comport” to “compare” here as well as on p. 9-127, line 23.

p. 9-103, line 14:

p. 9-104, line 8 of (3): change “is” to “are”.

change “McConnell” to “McDonnell”.

p. 9-122, line 8:

Shouldn’t both Pope et al. (1995) and Dockery et al. (1993) be cited here?

p. 9-123, line 24:

What is “ZPM”?

p. 9-126, line 19:

insert “for” after “serve”.

p. 9-133, line 6:

p. 9-136, line 13: insert “of reduced lung function growth” after “findings”.
insert “, 2002” after “2000”.

p. 9-136, line 15:

The “Ritz et al. (2002)” was not cited in Chapter 8. It’s OK to do so here, but it

p. 9-137, line 3:

should also be cited in Chapter 8.

p. 9-138, lines 23-28: The reader would get the false impression that the “~1.3 years” came from the Brunekreef paper. The real source of this estimate should be indicated.

p. 9-139, lines 6-10: This comparison was not in Chapter 8. Its source should be cited.

Dr. Joe Mauderly

Final Comments August 29, 3003

Review of Chapter 6: Dosimetry of Particulate Matter

General Comments

This chapter is basically completed. All the parts are there now, and past comments have been adequately addressed. There are errors in the calculations done with the interspecies extrapolation model, that need to be corrected and reviewed by Dr. Fred Miller. Otherwise, only a few minor edits remain to be done, as noted below.

Specific Comments

P6-15, L 30: This technique doesn't "measure" regional deposition, it provides an estimate. This problem, pointed out in last review, was fixed in other paragraphs, but this one was overlooked.

P 6-51, L 30: Here, the isotope (^{192}Ir) is given, but it isn't given for the Oberdörster study that used ^{13}C carbon particles. Be consistent one way or the other.

P 6-83, L 19-20 (and elsewhere): The descriptions of activity levels are confusing, and need to be made more consistent in the text, tables, and figures. Here, we have "moderately high activity level" and "lower activity level". These terms are different than those in Table 6-3, where we have "light exercise" and "heavy exercise". "Heavy" exercise in Table 6-3 is defined as 3 m³/hr, but it's defined as 3.54 m³/hr in Table 6-4. The figure legends for Figs 6-13, 6-14, and 6-15 need to define the exercise levels using terminology consistent with that in one or more tables. Presumably, the graphs in Fig 6-13 are for "moderately high exercise". How do "light exercise" and "resting" in Fig 6-15 legend relate to the terminology in the table(s)? Just go through the section and use some consistent terminology.

P 6-89, L 34: What is a "light" increase? Would that be like a "small" increase?

P 6-97, Fig 6-19, first graph panel: This panel shows 45% extrathoracic deposition for a 10 m particle in the rat. I didn't think 10 m was inhalable by the rat, or certainly not at 45%. At 5 m, it is nearly 60%, which also seems wrong. This is all part of the need to review all the interspecies model results in detail and ensure that the values presented are correct.

P 6-102, L 29: They are usually called "conducting" airways, rather than "conductive".

P 6-103, L 4: Is this supposed to mean that deposition doesn't increase with PM size this way in males? What's the evidence for that?

Review of Chapter 7: Toxicology of Particulate Matter In Humans and Laboratory Animals

General Comments

The treatment of doses is very inconsistent across the chapter. Doses, or exposure concentrations and times, are given for some studies but not for others. Considering that toxicological information has very little value without explication of dose or exposure parameters, any study that is worth citing must be worth providing doses. This point has been raised repeatedly in previous reviews, and is still not dealt with satisfactorily. It's a simple matter to go through the chapter and fix this.

There remains some confusion in the chapter between exposures to diesel emissions and exposures to diesel particulate. Those are quite different exposures. Effects of exposures to whole diluted diesel emissions (or any other complex combustion emission) cannot be ascribed to the particulate phase unless some specific steps were taken to prove that it was the particulate phase and not the gas or vapor phases that caused the effect. In contrast to common misperception, the particulate phase of diesel emissions comprises a very small portion of the total exposure mass concentration.

The endotoxin issue is not dealt with satisfactorily. It is discounted in some sections and highlighted in others. The in vitro section basically says that one of the NIST ambient PM samples, and many, if not most, of the other collected ambient PM samples contain endotoxin, and that endotoxin drives the cellular cytokine production. However, the summary of that same section doesn't even mention endotoxin. The overall summary in Section 7.7.1.8 notes that inhaled endotoxin has a threshold for "pulmonary and systemic" effects in healthy volunteers between 0.5 and 5.0 g, and that ambient levels do not exceed 0.5 ng/m³. Of course, CAPs has a pretty high threshold in healthy volunteers as well, yet the document doesn't take that as an indication that ambient PM isn't affecting people. You can't have it both ways – either endotoxin is an important component of ambient PM and the resulting health effects, or it's not. Either endotoxin is a sizable potential artifact in the toxicology information base, or it's not. On the other hand, if you are saying that it's important for in vitro studies, but unimportant overall because you don't believe those results can be extrapolated to humans, then why would you waste time extrapolating any other PM results from in vitro to humans?

The overall treatment of bioaerosols is pathetic. It remains a mystery why the CD doesn't deal with at least airborne allergens in any meaningful way, not even to mention the other bioaerosols. Unless the Agency believes pollens and other allergens all to be in the gas and vapor phases, they must be in the particle phase and they certainly have public health importance (and are certainly "environmental"). Surely you would not propose to convince the legions of allergic people that airborne biological PM or PM-bound materials are not important? Do you really believe, for example, that public exposures to ROFA have a greater overall public health impact than exposures to PM-borne allergens?

The “summary and conclusions” section at the end (Section 7.7) fails badly to live up to its title. A big contributor to this failure is that this section was apparently developed independently from the rest of the chapter. Very few of the subsections actually present a summary of the topic or present any high-level or “bottom line” conclusions. Several of the subsections consist only of descriptions of individual studies. Most amazingly, several of the subsections appear to describe studies that aren’t even described at all in the body of the chapter! One could question whether the author of this section even read the rest of the chapter in formulating the “summary and conclusions”. This section needs to be more than an afterthought – many readers might only read this part of the chapter. Of course, it’s harder to integrate complex and disparate information into a limited number of overall conclusions than it is to simply list studies, but that’s the need this section must meet. The need has not yet been met.

Specific Comments

P7-1, L 11: “Exist” should be “exists”.

P 7-2, L 15-16: Particles *per se* don’t form secondary aerosols. It is the non-PM materials that form secondary aerosols or adsorb to primary particles to change their composition.

P 7-3, L 20-22: A small number of subjects *per se* doesn’t justify high doses, unless you are trying to model only the most sensitive members of the larger population. Even then, the idea that high doses are justified on the basis of small group sizes is largely both a statistical and biological myth.

P 7-4, L 2: The suggestion that only “more recent” studies have used PM from bag filters is nonsense. The large body of research on coal fly ash collected from baghouses and ESPs goes back at least to the 1970s. Indeed, with the possible exception of EPA’s heavy investment in ROFA during the past 5 years, there was much more research on baghouse ash in the 70s and 80s than in recent years.

P 7-15, L 17: First, give a reference or two for the effects in rats and guinea pigs. Second, it is now believed that there is no such thing as “inert” particles; all particles cause effects at some dose. This is not useful terminology.

P 7-16, L 8: “Leukocytes” is misspelled.

P 7-16, L 12: Do you really mean 46 mg, or was it 46 g?

P 7-18, L 19: Here, a new terminology, “EPM” is introduced. Is this something different than ROFA (especially seeing that ROFA is very broadly defined in the chapter)? If you really mean to distinguish this stuff from other oil combustion-derived PM cited in the chapter, tell us what it is. If not, then don’t introduce a new term.

P 7-19, L 13-19: Give us some doses here. The table indicates dose in the 50-125 g range, so which doses caused effects (or did they all)?

P 7-19, L 25: It should be “—manner that is not —”.

P 7-21, L 18: It should be “—exposures to ambient—”.

P 7-21, L 28 & 30: The studies to which you refer used exposures to DE, not just DPM. The two are not the same.

P 7-22, L 2-5: Give citations for your conclusion that the effects of DPM are due to the “carbonaceous core” or metals. Certainly, the organic components of DPM, and even more so the total organic in DE, are inflammogenic. There is also evidence that the immune effects, which you aren’t citing here, are caused by both the organic and inorganic portions. Your conclusion, if well-founded, is meaningful, but you need to cite the evidence if convincing evidence exists. Of course, to be convincing, the evidence would have to show the effects from the components you list and show that the rest of DPM does not produce the effects or produces lesser effects.

P 7-24, L 1: The results of the Heinrich et al. 1980 study are not reported clearly. That was a study in which chemical carcinogens were administered to hamsters that were also exposed to diesel emissions (the use of carcinogens is not mentioned). In hamsters that were treated with carcinogens, more proliferations were observed in those also receiving whole diluted exhaust than in those receiving filtered exhaust. There was only one series that did not receive “extra” carcinogen. In that series, proliferations (not tumors) were observed in only 10% of the hamsters receiving whole exhaust, and in none receiving filtered exhaust.

P 7-27, 1st paragraph: This paragraph, while not untrue, is misleading. The Sandstrom group reported that, while asthmatics had these effects, the effects were not greater in asthmatics than in normals. That was an important finding, and should be portrayed correctly

P 7-27, L 25: Presumably, you mean combustion emission sources here. All PM come from “emission sources” of some kind.

P 7-30, L 10: You have already used the notation “NMRI” in the chapter. It should be defined the first time it is used, and then it doesn’t need to be defined thereafter.

P 7-31, L 28: Give doses or exposure levels.

P 7-37, L 15-16: This statement is not true. The 1996 CD did not conclude that bioaerosols “would not likely contribute” to the effects of PM; indeed the section noted that they might. What the 1996 PM CD did conclude was that bioaerosols “appear unlikely to account for observed ambient PM effects” (P11-36, paragraph 3). There is a big difference. Few, if any, suspect that bioaerosols completely “account” for the effects of PM, but most find it plausible that they might “contribute” to the effects.

P 7-39, L 4: Was there any information on the endotoxin exposures in the swine containment building? There are lots of things in the air of a swine containment building in addition to endotoxin.

P 7-45, L 3-4: Since it was noted earlier in the chapter that oil fly ash comprises no more than a trace of the urban PM composition, why do you call it a “model urban particle”? Was this stuff something different than ROFA (an abbreviation you use elsewhere)?

P 7-45, L 12-20: In this study, at which doses did they observe the effect? Studies using multiple doses are particularly useful for framing the dose-response relationship, and you note that the effect was dose-related. Go ahead and tell us which doses caused the effect and how much lower the effective dose was in the MCT rats (presumably the meaning of “exacerbation”). This information is much more important than the simple fact that effects were produced.

P 7-46, L 3-5: At what dose?

P 7-46, L 9: Why not use “ROFA” here, or is this yet something different.

P 7-48, L 21: “Produces” should be “produced”. The results can only be specific to the study that produced them – unless evidence from multiple studies makes it conventional wisdom.

P 7-50, L 3: Give us the dose.

P 7-50, L 24: I think it should be “Fischer” rats.

P 7-51, L 1-8: The author must have been tired at this point!

L 1: It should be “increased”.

L 3: It should be “Zelikoff”.

L 6: What are “match counterparts”? (they must be unusual – there aren’t any in all the studies cited in the rest of the chapter!)

L 7: It should be “was significantly”.

L 8: It should be “was reduced”.

P 7-51, L 22-31: What was the exposure pattern and concentration? What does “acute phase” mean – how long did the phase last? What was the instilled dose?

P 7-52, L 1-8: One can't understand the findings from the present wording. If the study determined whether or not the intensity of thrombosis was "modified", what was it to be modified from? What caused thrombosis in the controls? Where was the thrombosis? On what basis was it concluded that the effect was from PM "in the circulation"? Was circulating PM measured, or directly observed?

P 7-52, L 9-20: What was the exposure (time, concentration, etc.)? You bothered to list group sizes (which was rarely done for other studies cited in the chapter), but you didn't bother to describe the exposure!

P 7-52, L 23-25: Cite the "controlled human exposures". Are they described in more detail elsewhere in the chapter?

P 7-52, L 28-29: This is an interesting conclusion. I've heard Bob Devlin, Kevin Dreher, Mark Utell, and others present at national meetings reasonably convincing mechanistic "pathways" by which these effects likely occur. Indeed, there seems to be some evidence for numerous pathways, and a growing portrayal of confidence that sufficient pathways have been identified to explain the effects. I wouldn't argue that this is necessarily true, but in the presence of such proclamations, you need to explain what you mean by your statement that understanding pathways is "far from clear".

P 7-54, Table 7-8: Under chemical composition, why list pesticides? Or only pesticides? What about herbicides and the hundreds of other toxic chemicals and products?

P 7-54, L 2: Although in vitro studies typically use only one cell type, techniques are available to culture many cell types at once.

P 7-54, L 2-3: Actually the squamous epithelium in the anterior nose, and/or the oral epithelium, are the "initial target" of inhaled materials.

P 7-54, L 5-7: If you consider the limitations of: 1) dose; 2) extrapolation to in vivo; and 3) mechanisms, what is left? Based on this paragraph, one could argue that in vitro results shouldn't be summarized at all.

P 7-62, L 17: I wouldn't call ROFA an "ambient surrogate".

P 7-64, L 14: You are talking about a specific study, so it should be "—effects could be blocked—".

P 7-64, L 19-31: In effect, this section states that: 1) SRM 1648 is contaminated with endotoxin; and 2) endotoxin is a key cause of effects in both the NIST material and collected ambient PM. If this is true, it is a very important issue. Is this the same author that wrote page 7-37, where the importance of endotoxin is discounted? If it has been shown that endotoxin contaminates a common NIST standard and many ambient samples, and if it is also believed that endotoxin is

not important in the effects of real ambient exposures, then you have to conclude that much of the toxicological database is useless. You can't have it both ways.

P 7-65, L 10: Do you mean that the most potent fraction was the water-extracted fraction of PM10?

P 7-66, L 14-15: Here again, we have the statement that endotoxin is responsible for most of the cytokine activity of ambient PM samples. Without arguing whether or not that's true, I'd re-state that this section of the chapter is making the case for the importance of endotoxin, so that has to be one of the major conclusions from the chapter. If that is true, then why is that not a major conclusion of the CD?

P 7-66, L 22: "mice" should be "mouse".

P 7-67, L 4: "On human" should be "by human".

P 7-68, L 25-29: Based on the discussions of the importance of endotoxin in this section, it's incredible that endotoxin isn't even mentioned in the section summary! It seems that even the author of this section is of two minds regarding endotoxin.

P 7-69, L 9: "Discussed" should be "listed" – tables don't discuss.

P 7-69, L 14-18: This is an overly superficial and misleading treatment of the huge amount of data on mutagenicity of diesel, gasoline, wood, and other combustion emissions. Not even one reference is given! The issue of high vs low sulfur fuel is a red herring amongst all that information. As just one example, it would be more important to note that certain nitroaromatics seem to drive bacterial mutagenicity of combustion PM extracts. The statement about equal volumes of air or amounts of time isn't clear. Regardless, it is true that we know enough about the mutagenicity of airborne PM to know that a cancer effect is plausible.

P 7-71, L 16: Does mannitol inhibit DNA damage from all types of PM10? That's what the sentence implies, but I doubt that's known. Perhaps it's accurate to state that mannitol has been found to do so in some PM10 samples.

P 7-75, L 11: It should be "—AMs that were exposed--".

P 7-77, L 3: It's doubtful that PM is ever "trapped by impaction" in the epithelium (i.e., shot into the cells like bullets). Some of the deposited PM is "trapped" (i.e., not readily cleared) in the epithelial layer by multiple mechanisms which are still not totally resolved; however, it's very unlikely that it is trapped by impaction.

P 7-77, L 11: Be certain that "DRG" is defined, either previously or here.

P 7-80, L 23: "Involving" should be "involved".

P 7-85, L 8: What size were the particles?

P 7-85, L 15-16: This doesn't make sense. If acid droplets don't persist as particles, how do you propose they penetrate?

P 7-85, L 12-32: This paragraph is confusing, and the information appears to be in conflict. The point seems to be that ultrafine particles penetrate faster than fine particles, but it is also stated that one of the authors' assumptions was that that was not true. What is the point to be drawn from these results?

P 7-86, L 18-15: This information is confusing. You call one carbon black "defined granules" and the other "coarse structure". The meaning of neither term is at all clear. You conclude that particles of "single component" (another unclear term) produce greater response than "similar" particles with less surface. Apparently the particles were not similar at all. What's your point?

P 7-87, L 28: There are several other recent papers describing models. The series comprising vol 12(9) of *Inhalation Toxicology* should particularly be cited.

P 7-88, L 13: The description of the study says nothing about healthy animals, so how does the information demonstrate differences between healthy and MCT animals?

P 7-88, L 28 to 7-89 L 26: This information says nothing about PM effects – it just discusses models. Yet other models cited in the section are not described in such detail, but only describe PM effects. Be consistent.

P 7-90, L 13-29: The topic, or purpose, of this paragraph isn't clear. It starts by contrasting responses by age, then says "on the other hand" neutrophil influx wasn't found in MCT rats exposed to CAPs, then moves on to cardiomyopathic hamsters, and then back to MCT rats. The jumping from one topic to another prevents any point from being made clearly.

P 7-91, L 15: "Diffusion" should be "diffusing".

P 7-93, L 18 to 7-96, L 3: Other than pointing out that different animals may have different sensitivities, this section does little to summarize what is really known about genetic susceptibility. For example, on 78-94, L 11, C57BL/6 mice are called "non-responsive", on 7-94, L 26, C57BL/6 mice are the "most sensitive", and on 7-95, L 21, there is no strain difference between C57BL/6 and others. The point is not that this is in conflict, because the studies were different and the endpoints were different. The point is that the reader is left with no summary of what all that information might possibly mean about genetic susceptibility.

P 7-95, L 10: It should be "NiSO₄".

P 7-96, L 4, Section 7.5.3: Throughout this section, it is assumed that DE enhances asthma, or allergic asthma. Treatment with DPM or DE has been shown to alter certain immune and inflammatory responses in animals and in human noses, but this only confirms effects on “allergic asthma” if airway responses are measured. In the review and approval of the Diesel HAD, Dr. Diaz-Sanchez noted that changes in IgE (for example) did not equate to “asthma”. There is a need to be more precise about what we know and what we don’t, and what the different findings mean.

P 7-97, L 6: Use consistent terminology. Here we have “bronchio-alveolar lavage. In other places in the chapter we have “bronchoalveolar lavage”, “lavage”, “lavage fluid”, and BAL.

P 7-97, L 18: What was the dose?

P 7-97, L 24: What was the exposure (conc. and time)?

P 7-98, L 6: What was the dose?

P 7-98, L 21: What was the dose?

P 7-99, L 4: What was the dose?

P 7-99, L 15: How do you draw conclusions about gases, when the preceding studies used instilled DPM?

P 7-99, L 22 and 24: In one place you say the subjects were exposed to DPM, and in another it’s DE. If the exposure is to DE, then you need to say it was to DE diluted to some PM mass concentration. DPM and DE are very different exposures.

P 7-100, L 1-3: The “fact” that number concentrations are going up as diesel PM mass is decreasing is largely, if not totally, a myth. If you have facts showing otherwise, give a reference.

P 7-100, L 10: What was the exposure?

P 7-100, L 24: What was the exposure?

P 7-101, L 10: “The” should be “that”.

P 7-101, L 14-22: The reader can’t understand the study from the information given. L 14 indicates that 1 mg of ROFA or specific metals was administered, but later it indicates that the metals were given at concentrations equivalent to their presence in the ROFA. For the citation to have value, tell us how much of each was actually given and what form the metals were in.

P 7-101 L 29: What was the dose?

P 7-102 L 31: What was the dose?

P 7-109, L 22-23: The missing point here is whether or not the effects were greater than additive. There are no “interactions” unless the effects are different from additive.

P 7-110, L 8: What was the exposure time? One doesn’t know the exposure unless you know both the exposure concentration and time.

P 7-110, L 18: Was it greater than additive?

P 7-110, L 30: Does “synergistic” mean more than additive?

P 7-111, L 1: These results, and the intent of your citation of them, are not clear. One exposure caused metaplasia in the nasal transitional epithelium, another caused metaplasia in the conducting airways, and the third caused metaplasia in the maxillary turbinates. What sense are you trying to make by comparing these different effects?

P 7-111, L 30: “With” should be “with”.

P 7-112, L 1-13: How could you compare these different exposures, and conclude that the difference was due to lab vs ambient?

P 7-112, L 14 to 7-113, L 16: No exposure information is given, so what sense can you make of it? How can you infer anything about PM effects, when there were hundreds of air contaminants present, and some studies had no measures of exposure at all?

P 7-114, L 13 (entire summary section): This is hardly a summary (of the foregoing) at all. Indeed, the evidence suggests that this section must have been developed completely independently from the foregoing material. It cites studies (sometimes describing them in detail and sometimes not) that are not even cited in the relevant sections of the preceding text. As to conclusions, there are very few high-level conclusions that integrate the foregoing material. This section is important, not only because many readers might read only this part of the chapter, but also because writers of Chapter 9 or the Staff Paper might only read this section. It’s not well done.

P 7-115, L 15-16: It’s true that such comparison ought to be made, but you don’t do so in this section, or indeed in the entire chapter. It is noted in several places that the laboratory exposures were higher than ambient, but there is nowhere in the chapter that notes specifically the lowest ambient, CAPs, DE, ROFA, or other PM exposure observed to cause effects to date, and how those exposures might relate to equivalent human exposures. That would be both useful and easy to do, but the chapter dodges that responsibility. If such information is not going to be integrated, then there was little use for including chapter 6 on dosimetry.

P 115, L 30-31: It's odd that this was not even mentioned in the section on acid aerosols. If there is a rationale why acidity is not important, expand on it.

P 7-116, L 2-3: It's also odd that the Zhang citation was not even mentioned in the section on acid aerosols, nor was the citation listed in Table 7-4. This is supposed to be a summary chapter, not a place to introduce new studies.

P 7-118, L 14: There are many different kinds of carbon black. The relevant point is not just that the composition might vary with particle size, but that carbon blacks are not all the same. Particle size is just one of several variables.

P 7-118, L 15: Something is wrong with the wording. Maybe it should be "used as a dose metric".

P 7- 118, L 17-21: The connection among these three sentences is not clear.

P 7- 119, L 15: This section doesn't mention that PM can carry bio-derived materials, and thus comprise "bioaerosols". What about the Knox et al., 1997 citation on page 7-96? Isn't this an important point? Endotoxin isn't the whole story.

P 7-122, L 1-20: There is no "summary" at all in this section; it is just a description of two studies. Moreover, neither of these studies is mentioned in the preceding Section 7.5.4 on respiratory infection.

P 7-122, L 22-31 and 7-123, L 1-3: This section needs a simple statement as to whether or not there is experimental evidence that CAPs alters immune responses. From the preceding sections, there is apparently not much evidence, which is amazing considering the number of groups exposing animals to CAPs.

P 7-124, L 1-24: This section needs a summary and conclusions, instead of describing a couple of studies in detail. That detail should go in preceding sections. Here again, we have a study "showcased" (Wellenius et al., 2002) that isn't even mentioned in preceding sections. It should be described in Section 7.3 or 7.5.

P 7-126, L 1-21: This is way too much detail for a "summary". Once again, we have two studies described in detail in a "summary" that aren't described in preceding sections. This material should go into Section 7.4.4. It is also interesting that the "Technigas" study is showcased here in the summary, when there is considerable question about whether the label actually stayed with the particles.

P 7-127, L 24 to P 7-128, L 6: These studies shed no light whatsoever on interactions between PM and co-pollutants. They are simply studies of ambient air pollution, and the composition exposures are either poorly described, or not described at all.

P 7-128, L 7-14: Neither of these studies shed light on interactions. As I recall, the Brook et al. study included PM and ozone, but made no attempt to study interactions, or even the effects of individual pollutants. The Linn et al. study came closer to studying interactions, but demonstrated none. Overall, this section misses the point, as well as lacks any “summary” or conclusions.

Review of Chapter 9: Integrative Synthesis

General Comments

This chapter is quite variable in the quality of writing and stage of editorial correctness. Up to section 9.8.1.2, it is still quite rough, and contains numerous sentences that make questionable sense. From that section forward, it is in much better shape.

Overall the chapter is not a serious attempt at an integrated summary. It is written as a summary of different topics and contains very little in the way of integration across topics to reach “bottom line” conclusions. There is no final synthesis or collection of conclusions at the end. If the summaries at the end of the individual foregoing chapters are done well, there is no reason to reiterate the material here.

I may be most appropriate to use those portions of the chapter that comprise adequate summaries to enhance the summaries of individual preceding chapters, and to create a chapter 9 focuses solely on integration across topics. There are several broad topics, or questions, to which multiple foregoing chapters pertain, and this chapter should be organized around those topics.

The following specific comments are offered, realizing that much of the text may be dropped altogether.

Specific Comments

P 9-20, Figure 9-7 legend: It is not clear why it would necessarily be “optimal” to remove all PM-bound water, but not other materials adsorbed to PM. First, if people inhale PM containing water, that’s the material we need to study and understand. Second, the material reaching the lung will all be equilibrated with water at body temperature before it deposits anyway. Third (and most importantly) drying off the water is likely to also change the balance of semi-volatile materials between the particle and vapor phases. Of course, the benefit is a more uniform way to measure mass. However, the potential artifacts should at least be mentioned.

P 9-34, L 7-8: It is not clear why co-pollutants could only be confounders if they cause the same effect. Why could not a co-pollutant be a confounder if the effect is only caused when the exposure includes PM and the co-pollutant; i.e., both are necessary for the effect but neither are sufficient? Just as is true for the epidemiology chapter, the section on confounding here is not very helpful.

P 9-35, L 11-13: The meaning of this sentence is not clear. Does it mean that there are exposure studies but that the studies did not include health outcomes? It must not mean that there have not been epidemiology studies of the co-pollutants, because there have. I'm not certain whether it's the wording or the concept that is confusing.

P 9-38, L 31: The reference to a specific brand name should be deleted. Brand, or proprietary, names are not used elsewhere. The point is not the brand, it is the class of material the brand contains.

P 9-43, L 14: You must mean greater total respiratory tract deposition fraction. Surely total deposition would still be higher in adults.

P 9-44, L 1: "Breath" should be "breathe".

P 9-44, L 18-20: This sentence is not quite right, although your thought may be. There are different dose metrics. Deposited dose is not affected by clearance, but retained dose is. Dose *per se* is not affected by species "sensitivity", although it varies among species. Sort out the different thoughts.

P 9-44, L 22-23: This sentence doesn't make sense. The higher deposition "density" (whatever that means) is not just because the lungs of rats are smaller. First, "deposition" could not be similar in rats and humans, but "deposition fraction" could be (but isn't). If the deposition fraction were the same, the deposition "density" (if you mean deposition rate per unit of respiratory tract mass or surface) would depend on the relationship between ventilation rate and lung size. Because rats have a higher metabolic rate than humans and ventilate at a greater rate per unit of size, then deposition density would be higher in the rat. The point is that the size of the lung is only one of the factors causing the difference. The relative deposition fractions and ventilation rates are the primary drivers.

P 9-50, L 22-25: The whole terminology about "region of origin" seems to cloud the issue. It's the sources that determine composition, and of course some sources vary by region. The wording "—general composition of generic PM in that classification mode—" is incomprehensible. What in the world is "generic" PM?

P 9-51, L 4-6: The fact that there is not a single "magic bullet" doesn't mean that sources are the best linkage to PM effects. There are many "magic bullets", and we need to understand them. If you are saying that doing so is a waste of time and we only need to link effects to sources, then EPA will have to do a much better job of looking at sources (all of them) than in the past. The take home message here wouldn't be clear to anyone not intimately involved in the science and related debate, and it's not very clear to those.

P 9-51, L 11: The sentence doesn't make sense. What does it mean to "separate physicochemical attributes" from "mechanisms"?

P 9-51, L 21-22: This is unclear. What does “uncertainty and narrow range of responsiveness” mean?

P 9-52, L 9-10: How do you interpret the NRC agenda as meaning that one, or perhaps a few characteristics are important is “inherent”?

P 9-53, L 24-26: Here we have four terms for the same thing in one sentence! First it’s “cars”, then “vehicles”, then “vehicle”, then “traffic”. This is supposed to be a clear, readable synthesis.

P 9-54, Table 9-7: “Sulfate” is not a “source category”.

P 9- 55, L 13-16: I can’t possibly understand what this sentence is saying, but whatever it is, it certainly doesn’t belong in an integrative summary!

P 9-55, L 56: The fraction doesn’t “comprise” the constituents, the constituents comprise the fraction.

P 9-55, L 28-31: This thought doesn’t make sense. Just because the accumulation mode presents (or accumulates) most of the absorptive surface and therefore carries most atmospheric reaction products doesn’t at all mean that the coarse mode doesn’t also carry those materials. It just means it carries less.

P 9-56, L 5: Since a “surrogate” could be anything, why does it follow that “earthen-derived” PM would necessarily be less toxic than a “surrogate”?

P 9- 56, L 22-23: “Sparked carbon” is an interesting new term. Presumably you mean carbon particles generated with an electric arc generator. In all the material I’ve seen on carbon generated by an electric arc generator, this is the first time I’ve run into this term. No need to invent new jargon in this chapter.

P 9-57, L 21: I think you mean “electrocardiogram”.

P 9-59, L 14: Delete the last sentence about organics. This paragraph is about inorganics.

P 9-60, L 8: The need is not just to determine the potential contribution of diesel exhaust, but to determine the contributions of all different PM, including the other mobile source-derived PM which undoubtedly acts like diesel, but nobody has looked.

P 9-60, L 15: Whether or not the biologicals “account” for the effects is not the point. Nobody conjectured that they might “account” for them. The point is whether the contribute to the effects, which is a very good bet. This terminology was cleaned up in Chapter 7, but apparently this author missed the correction last time around.

P 9-60, L 13-29: This whole section portrays endotoxin as the only “biological constituent” of concern. Just how many airborne allergens are not in the PM fraction? This falls short of a serious treatment of the topic.

P 9-61, L 4-7: This sentence doesn’t make much sense. Of course there is not a single “primary” attribute. However, that doesn’t mean that all PM effects are the aggregate outcomes of many attributes. There can be many attributes that are “primary” for different effects.

P 9-63, L 7-8: HRV does not have to be either an “independent risk” or a “marker of exposure”. If it is important it is most likely a contributing, underlying, or predisposing factor to an important outcome, but not the “primary” factor.

P 9-63, L 31: It is spelled “Ottawa”.

P 9- 64, L 4: It is still spelled “Ottawa”.

P 9-64, L 10: It should be “—nerve endings--”.

P 9-64, L 22-24: Why bring up asbestos, unless you are talking about ambient asbestos that falls within PM10. There is now lots of evidence that particles go to organs outside the lung. There is no need to drudge up this irrelevant example.

P 9-64, L 29: I don’t think that ROFA is made up of “mostly” soluble transition metals. It contains a lot of soluble transition metal, but I don’t think that comprises the bulk of the mass.

P 9-65, L 29: The exposure was to CAPs and ozone. No work was done to determine which pollutant caused the effect, or if it required both.

P 9-68, L 23: “Health” is used redundantly in the sentence.

P 9-69, L 1-2: The fact that the effects were not statistically significant could reflect two circumstances: a lack of statistical power, or a real lack of significant effect.

P 9- 69, L 20: It is also possible that effects of the “other toxic agents” could be mistakenly attributed to PM.

P 9-70, L 1-15: This material is repetitive. Indeed, there are several concepts that are repeated throughout the chapter up to this point.

P 9-71, L 22-30: I know the use of different denominators for different particle sizes now has a strong history in EPA documents, but it remains confusing. Since these are just slopes anyway, and have little if anything to do with absolute PM concentrations, why not just describe risks using the same mass metric for the “denominator”? That would make things less confusing for the public (and most of us).

P 9- 126, l 19: Is “ZPM” defined somewhere, or is that a typo?

P 9-132, L 13: The exposure was to CAPs and ozone. Don’t portray the response as an effect of just CAPs.

P 9-136, Table 9-13: The meaning of the asterisks in the data columns is not given.

P 9- 136, L 10: Did the Plopper and Fanucchi study include PM exposures? I know they have been working with ozone, but the implication of including it here is that they also have evidence for PM.

P 9- 137, L 4: What in the world does “inconclusively linked” mean? Does that mean there was no effect or that there was an association that did not reach statistical significance?

P 9-151, L 12: Don’t you mean “concretes” instead of “cements”? They are not the same.

Dr. Roger O. McClellan

Comments on EPA Fourth External Review Draft of Air Quality Criteria for Particulate Matter (June 2003)

Roger O. McClellan
Advisor: Toxicology and Human Health Risk
Analysis
13701 Quaking Aspen Place NE
Albuquerque, NM 87111

Summary Opinion of Reviewer

In this reviewer's professional opinion, the 4th Draft of the Air Quality Criteria for Particulate Matter (June 2003) (CDPM) is an improvement compared to earlier drafts as a compendium of information on particulate matter and its effects on human health and the environment compared to earlier drafts. However, the CDPM is not an adequate compilation, synthesis and analysis of the scientific criteria required under the Clean Air Act for review and establishment of National Ambient Air Quality Standards for PM. Specifically, the CDPM fails to clearly present and interpret the scientific evidence bearing on the four key elements of the NAAQS for PM, namely: (a) the identification of potential indicators such as PM_{2.5}, PM₁₀, PM_{10-2.5}, etc; (b) the averaging time, (c) the numerical level, and (d) the statistical form. Beyond failing to present, synthesize, analyze and interpret the science bearing on these four elements, the present compendium in many places presents the scientific information on PM in a biased manner that may mislead individuals charged with making policy decisions on the NAAQS for PM.

In my professional opinion, the most serious deficiencies in the CDPM are as follows:

1. The CD overstates the evidence for an association between ambient PM at levels typically found in the United States today and increases in morbidity and mortality.
2. The CD understates the role of gaseous components of air pollution in increasing health effects in favor of exaggerating the role of PM.
3. The CD fails to clearly relate the weight of the evidence of an association between PM₁₀ and adverse health effects, overstates the weight of the evidence for an association between PM_{2.5} and adverse health effects and very substantially overstates the evidence available on association between PM_{10-2.5} and adverse health effects.
4. The CD frequently relates the theme that PM is PM is PM irrespective of its chemical composition while never clearly stating that the evidence, while collected in an *ad hoc* and non-systematic way, points to marked differences in the toxic potency of various kinds of PM of varied chemical composition.

5. The CD repeatedly implies that PM of combustion origin all has the same toxic potency. The CD fails to relate the remarkable differences between different kinds of PM of combustion origin, i.e., coal combustion for electrical generation with 1950s versus 1980s versus 2000 technology, diesel locomotives with 1950s versus 2000 technology, diesel trucks and buses with 1950s versus 1980s versus 2003 versus 2003 prototype technology, forest fires, open field burning, uncontrolled versus controlled fire places, etc. While all of these are combustion processes, they do not produce identical PM emissions. It is remarkable that EPA has never critically examined this assumption since it under-girds the Agency's entire regulatory program for PM.

6. The CD fails to relate, analyze, synthesize and interpret the substantial data showing that sulfates, a primary mass component of emissions from modern coal-fired power plants, have very low toxicity.

7. The CD fails to adequately discuss and interpret the information available on exposure-response relationships for various PM indicators. Instead, the document adopts the use of linear exposure-response models without adequately stating the weaknesses in the evidence. The discussion focuses on statistical tests of linearity versus non-linearity without considering other approaches. For example, the lack of statistically significant positive associations between PM₁₀ and cardiorespiratory mortality in all but two cities in the National Morbidity and Mortality Air Pollution Study (NMMAPS) provides strong empirical evidence for a practical threshold for PM₁₀ at the PM₁₀ air concentrations measured, in those cities.

8. The CD consistently over-interprets the evidence for a causal link between various PM indicators and adverse health effects by using the results of experimental studies conducted with very high levels of exposure to non-representative PM and frequently using non-physiological modes of administration of PM.

9. The results of the epidemiological studies using Generalized Additive Models (GAMs) with appropriate convergence criteria are consistently over-interpreted by making reference to past flawed analyses. The past flawed analyses have no standing nor relevance and should not be used to prop up the weak associations found with proper analysis.

10. The document frequently fails to distinguish between proposed hypotheses or assumptions based on experimental results and instead erroneously relates the conclusions as though they were proven facts.

In summary, the manner in which the CD is organized and the tone of the CD does not provide scientifically sound criteria for decisions on indicator(s), averaging time, level and statistical form of the NAAQS for PM. Indeed, the nature of the presentation is such that it may mislead some policy makers.

As a postscript, I urge the Agency to give careful consideration to the public comments offered on the 4th Draft of the PMCD. In some cases in the past, Chapter authors totally ignored “public” comments. Many of the comments were excellent and provide a perspective absent in many chapters. It appears that some chapter authors, especially the authors of Chapters 7 and 8, treat the public comments as something EPA should deal with in some minimal manner after the CD is finalized. This is not appropriate.

General Comments on Executive Summary

As noted earlier, the total document would be substantially improved if the approach to review, synthesis and integration of the scientific information on particulate matter were to focus on the four essential elements of a National Ambient Air Quality Standard, namely; (a) identifying potential indicators such as PM_{2.5}, (b) the averaging time, (c) the numerical level, and (d) the statistical form. It would be of substantial benefit to agency decision-makers, the public at large, and other interested parties if key scientific information bearing on selection of these four elements were summarized in the Executive Summary. Indeed, I interpret the language of the Clean Air Act to call for an exposition of the scientific criteria that under-girds these elements rather than the creation of an encyclopedia of information on air quality and particulate matter.

The existing version of the Executive Summary is excessively long, containing considerable extraneous information and lacking certain key information.

Specific Comments on the Executive Summary

pg E-3, item 5/6: The statement that “fine PM is derived primarily from combustion material” is dogma. I do not believe the statement is supported by a quantitative analysis anywhere in the document.

pg E-4, item 1: Include a statement defining both PM₁₀ and PM₁₀₋₂₅.

Section E.2.2: This section should include a statement as to the current adequacy of knowledge on PM source characterization. It is my impression that knowledge in the area is inadequate and has not been substantially improved during the past five years. (Fourth NRC PM report).

pg E-6, item 3: The statement that coarse particles tend to have more localized effects than fine particles may be true. However, this section should focus on transport and fate and not prematurely delve into effects issues. Perhaps the sentence should be rewritten to emphasize major variations in coarse PM concentrations over short spatial and temporal dimensions.

pg E-6, item 9: The summary needs to emphasize that a Federal Reference Method does not exist for coarse PM (PM_{10-2.5}). In addition, it should be noted that the subtraction method yields very impressive results.

pg E-9 at about items 5 & 6: Information should be provided on PM10 concentrations.

pg E-9, item 7: The first sentence is unclear.

pg E-9, item 8: The statement “Data for PM10-2.5 concentrations are not as abundant as they are for PM2.5” is grossly misleading. A more correct statement is “Data from PM10-2.5 concentrations are very limited and highly uncertain.

pg E-10, item 14: Statement should be qualified in quantitative terms, most people spend about 90% of their time indoors.

pg E-11: Need a statement on impact of air conditioning. Need a statement on regional variations in heating, air conditioning and home construction practices.

pg E-13, item 30: This is a speculative statement that should be identified as such.

pg E-13, item 31: This is a highly speculative and biased statement.

pg E-14, items 2-10: These very terse statements do not adequately convey the status of knowledge in this area.

pg E-15, item 2: I do not think the terms- absorptive and non-absorptive - are commonly used terms.

pg E-15: This section needs to be rewritten in an understandable and informative format.

pg E-16, item 6, line 4: The word “comparable” should be replaced by “similar.” Throughout the document the word “comparable” is misused when the more appropriate word would be similar. Many items can be compared, only some items are similar.

E-4. Toxicology: This section should start with a statement that very few systematic studies have been conducted in either laboratory animals or human subjects to compare the toxic potency of major PM constituents. It should then proceed to note that comparison of the results of independent studies of different kinds of PM suggest that PM from different sources and of differing composition varies markedly in toxic potency.

E-17, item 1: This is a sweeping statement that is not true. Particles from different types of combustion of different fuels vary markedly in metal content. The Utah Valley situation is a very unique situation and care should be taken in relating it a prototype for combustion sources or even other steel mills.

E-17, item 2: The statement “There is growing toxicological evidence that diesel exhaust particles exacerbate the allergic response to inhaled antigens” is not correct.

E-4: Toxicology: This section should include a statement that most toxicological studies have been conducted with large doses or high exposure concentrations and frequently with non-physiological modes of administration that introduce the need to make extrapolations, that are highly uncertain, to human breathing ambient concentrations of PM. A statement should be made noting that very few animal or controlled clinical exposure studies have been conducted with multiple exposure/dose levels that are necessary to inform consideration of exposure (dose)-response relationships.

Section E.4.2. Mechanisms of Action: This section should begin with a statement that understanding of the mechanisms of action of PM of varied composition and at differing exposure levels is only beginning to evolve. At this stage, it is possible to postulate a range of hypotheses. However, few of the hypothesized mechanisms of action have been rigorously evaluated.

E-5, Epidemiology: In my opinion, this section over-states the current status of the epidemiological evidence of the association between ambient PM and adverse health outcomes. It appears to understate the role of gaseous pollutants in air pollution associated effects and understates the uncertainties in current knowledge of PM associations.

The summary statements do not adequately address the issue of exposure-response relationships. Linear no-threshold exposure-response models are embraced without adequate discussions of alternative models and uncertainties.

The statements offered should be factual and speculation should be eliminated. An example of an in appropriate linkage of fact and speculation follows (pg E-23, item 4):

“There appears to be some spatial heterogeneity in city-specific excess risk estimates for the relationships between short-term PM₁₀ concentrations and acute health effects. The reasons for such variations in effects estimates are not well understood at this time, but do not negate ambient PMs likely causative contributions to observed PM-mortality and/or morbidity in many locations.” The use of phrases like “probably contributing cause” are speculative and misleading.

E-23, item 6: The statement “A smaller body of evidence appears to support an association between short-term ambient thoracic coarse fraction (PM_{10-2.5}) exposures (inferred from stationary air monitor measures) and short-term health effects in epidemiologic studies” is very misleading. A more accurate statement would be – “A very limited body of epidemiological evidence is available on the association between ambient PM_{10-2.5} concentrations and adverse health outcomes. Some studies show a statistically significant association, other studies do not demonstrate an association.”

E-24, item 8: Any discussion of chronic exposure effects and, especially lifetime exposures, must acknowledge the difficulty of establishing the relevant exposure metric in the denominator of the calculation. The majority of mortality in such situations represents deaths of individuals

whose exposure extended to the 1920s to 1940s when air pollution was substantial in many cities in the U.S. The use of exposure metrics, even from a decade or two ago, markedly overstates the “risk” per unit exposure concentration.

Section E.5.2, Key Epidemiological Findings: I suggest the time has arrived when exposure-response functions (when given in a linear form) be stated as response per : g PM_x/m³. The introduction of arbitrarily selected normalization units such as per 10, 2.5 or 50 : g PM_x/m³, is confusing and potentially misleading.

pg E-27, item 1: I strongly support the statement – “The above reasons suggest it is inadvisable to pool PM epidemiologic studies for different locations or time periods, with different population subgroups, or different health endpoints (as is often done in “meta-analysis”), without careful assessment of potential causes and consequences of these differences and appropriate caveating of results,” Indeed, I would prefer a strong statement urging that extreme caution should be exercised in making any “body count” estimates recognizing the current uncertainties in our knowledge of exposure-response relations for PM_x.

pg 3-41, item 6: This statement should be prefaced by a statement that most epidemiological investigators of air pollution have used relative risk models. With these models the excess risk is directly related to the level of risk in the subpopulations presenting the underlying level of risk in the population under study. Hence, if most cardiopulmonary morbidity and mortality in a population is observed in smokers or former smokers, then the excess statistically calculated risk is related to this subpopulation. The “signal” of excess risk attributable to air pollution is so small that it is not possible to establish whether or not other new susceptible subpopulations are “affected.”

pg E-41, item 10, lines 5-9: I strongly endorse the statement- “In view of geographic differences in ambient PM mixtures and demographics, broad generalization of some single “best estimate” of relative risk for a given increment of a given particle indicator (e.g., PM₁₀, PM_{2.5}, etc.) would be subject to much uncertainty.” As noted earlier, the calculation of “body counts” should be strongly discouraged.

pg E-42, item 17: This statement and especially: “these studies lend confidence that further reductions of ambient air pollution exposures in the U.S. would reduce both respiratory and cardiovascular health effects” represents a very bold statement that is difficult to support. If it is retained it needs to be supported by a detailed analysis elsewhere in the document. Further, it would be well to note that since air pollution has a very small impact compared to other risk factors, such as smoking and diet, for respiratory and cardiovascular health effects, it will be difficult, and perhaps impossible, to detect any reductions if they occur.

pg E-42, item 17: Caution should be exercised in any generalization of the Utah Valley experiences.

pg E-44: This concluding statement is not well supported and is misleading. The emphasis needs to be on PM as one of the measured components of air pollution. To say it is the ‘primary contributor to a variety of adverse health effects associated with air pollution’ goes beyond current knowledge.

General Comments on Chapter 1. Introduction:

Very early in this chapter, a paragraph is needed to describe the four elements that comprise a National Ambient Air Quality Standards, namely, (a) an indicator, such as PM_{2.5}, (b) an averaging time, such as 24 hours, (c) a numerical level, and (d) a statistical form. I submit that the criteria document would be much shorter and more useful if all of the authors had been asked to review, synthesize and integrate knowledge bearing on these four elements. In the absence of such an assignment the result is an encyclopedia of data, most of which is irrelevant to provision of criteria for establishing a NAAQS for PM. I am not challenging that the science that is irrelevant to setting the NAAQS does not have value nor is not of interest. Those are separate matters.

It would be useful for the Introduction to have a paragraph or two that traces the historical development of concern for air pollution and the setting of standards to regulate air pollution. It would be useful to note the strong linkage between “regulatory compliance-based air monitoring” and the conduct of epidemiological investigations. A statement of the obvious would be very useful – you can only study associations between what has been monitored and health effects that have been documented. It would be useful to note how this impacts on the information base for decisions on indicators for PM; substantial information on PM₁₀, limited information on PM_{2.5}, almost no information on PM_{10-2.5} and essentially no information on other potential indicators.

General Comments on Chapter 2. Physics, Chemistry and Measurement of Particulate Matter

Fig 2-6: The curve for PM₁₀ does not appear to have been appropriately plotted. If it is plotted appropriately because it is expressed as percent of the inhalable PM curve, then this should be explained in the text.

General Comments on Chapter 3. Concentrations, Sources, and Emissions of Atmospheric Particulate Matter

It would be very useful if a section could be added to this chapter to relate whatever information is available on air quality measurements extending to the mid-1900s. It would be especially useful if data could be found for the communities included in the Six Cities studied by the Harvard Investigators. This would aid in interpreting the results of the Six Cities study in which chronic effects observed in recent decades may be in part related to exposures occurring early in the life of the cohorts studied. Likewise, it may be useful for completeness to include

the summary of monitoring data given in the updated analysis of the American Cancer Society cohort by Pope and investigators.

Specific Comments on Chapter 3

pg 3-104: The statement on PM_{10-2.5} should be more direct – “Very limited data are available on ambient concentrations of PM_{10-2.5}. Most of the available data are based on differences between measured PM₁₀ and PM_{2.5} and are very imprecise.”

pg 3-104: The issue of background concentrations of PM_x needs more discussion in the text and in the chapter summary.

pg 3D-15, line 9: Diesel engines are internal combustion engines. Did the authors mean “either diesel or gasoline fueled engines”?

General Comments on Chapter 5. Human Exposure to Particulate Matter and Its Constituents

This is a well-written and informative chapter. It would be useful if the chapter were to more clearly indicate the very limited amount of information available on ambient PM in enclosed workplace environments. Most of the progress in obtaining measurements of PM_x in the “built” environment is for private residences and special facilities such as nursing homes. Very little information is available for work place environments.

I strongly endorse the statement (pg 5-122, lines 3-5): “As yet, there is no clear consensus among exposure analysts as to how well community monitor measurements of ambient air PM concentrations represent a surrogate for personal exposure to total PM or to ambient PM.” The statement should be included in all summary statements prepared for the document.

General Comments on Chapter 6: Dosimetry of Particulate Matter

This chapter is generally well written although it is apparent that material has been added that is not well integrated into the original text. In addition, the chapter still does not contain an adequate exposition on estimated deposition for various exposure scenarios (particle size, exposure duration, etc.). This information was previously requested to aid in comparing the results of experimental studies with anticipated human deposition from exposure at ambient concentrations of PM.

Specific Comments on Chapter 6

pg 6-53: The results of Numnar *et al.*, 2002, and the other studies with labeled PM need more discussion as regards the issue of the tracer being a true tracer for PM when evaluating extra-pulmonary translocation.

pg 6-65: The statement that “an instillation of 150 : g could be reasonable” is not adequately supported. What the authors fail to grasp is that 150 : g instilled into a rat lung is the equivalent of 13,500 : g into a human lung. Moreover, not just a few cells receive the heavy exposure but a very large number of cells.

pg 6-66: The attempts to justify the use and interpretation of the instillation studies should be toned down.

General Comments on Chapter 7: Toxicology of Particulate Matter in Humans and Laboratory Animals

There are serious problems with the present draft of Chapter 7. An over-arching issue is the failure of the chapter to indicate the potential value of toxicological data for decisions on the selection of indicators for a PM NAAQS. Unfortunately, very little research has been performed in a manner that allows interpretations to be rendered on the comparative potency of PM fractions differing in size distribution or chemical composition. The limited data available from studies of different PM fractions can generally only be interpreted in very qualitative terms. The focus has been on trying to identify a few “hot samples” such as ROFA and then study them intensively even if not very representative of the “world of PM.”

Only very rarely have studies been done in a manner that allows rigorous comparisons to be made of the relative toxicity of different PM fraction. In addition, few studies are available with multiple exposure levels that would have allowed rigorous evaluation of exposure-response relationships including non-linear exposure-response relationships. Most of the studies reported have used extraordinarily “high exposures/doses,” frequently with non-physiological modes of administration such that it is difficult to interpret the relevance of findings to humans exposed at ambient concentrations of PM.

In my opinion, the chapter systematically over-interprets the available data on toxicological modes of action and the relevance to human exposures at ambient levels. The chapter fails to adequately convey the substantial uncertainties that remain with regard to understanding the potential toxicity of various kinds of PM at ambient concentration levels. The case for coherence of the toxicological and epidemiological data on PM is strongly dependent on the implied assumption that PM is PM, irrespective of its chemical composition. The chapter treats this assumption as though it is “proven,” which it is not and implies that the results of a few studies with unusual composition such as ROFA or some of the CAPS somehow have relevance to all PM.

In several places, the chapter references research done on diesel exhaust particles. In some cases the studies are not adequately described and/or are inappropriately interpreted. Since the Agency only very recently released a Health Assessment Document on Diesel Exhaust I suggest most, if not all, of the references to diesel exhaust exposure be removed from the CD and instead cite the diesel Health Assessment Document. It is certainly inappropriate to cite a review draft of the document as done on pg 7-23, line 27.

If any diesel references are retained care should be taken to specifically identify the engine, fuel and exhaust treatment system used to produce the diesel exhaust and the PM exposure concentrations. If exposure concentrations are unknown, such as Rudell *et al*, 1999 (see pg 7-22, lines 12-28) then the study is not worth citing.

General Comments on Chapter 8: Epidemiology of Human Health Effects Associated with Ambient Particulate Matter

This chapter, while improved from the original version, is still not an adequate review and interpretation of the available epidemiological literature for establishing criteria for setting the four elements of a PM NAAQS. In my opinion, the tone of the writing is to emphasize “certainty” and underplay the substantial “uncertainties” that exist in estimating the health risks of exposure to PM in different parts of the U.S. at PM concentrations in the ambient range.

In my opinion, the chapter has the following deficiencies.

(a) The chapter systematically overstates the weight of the evidence for elevated PM levels being associated with increased levels of PM and understates the uncertainties in the data. This is especially the case for the very limited amount of PM_{10-2.5} data.

(b) The chapter systematically overstates the degree of coherence in the total data base on PM playing a “causal role” in increases in health effects.

(c) The chapter fails to adequately convey how small and uncertain the signal is for a PM-associated health effect and the difficulty of characterizing PM as a “risk factor” compared to other much more substantial risk factors.

(d) The chapter does not adequately address the issue of confounding, especially by gaseous co-pollutants and overstates the case for dismissing gaseous pollutants. Part of the dismissal process is the forcing of all data into a one size fits all, it is PM, for the entire U.S. The role of “socio-economic status and education” are not adequately dealt with despite their importance as shown in the Krewski *et al.* reanalysis of Pope *et al.* Weather as a confounder is not adequately addressed.

(e) The issue of alternative models for exposure-response relationships is not adequately addressed. Again the issue is a tendency to seek to force the emergence of a best model when multiple models need to be considered and different models may be most appropriate for different data sets for different regions of the U.S.

(f) The chapter overstates the strength of the evidence on susceptible populations. The role of cigarette smoking as the major contributor to the baseline of respiratory and cardiac disease deserves much more thorough discussion.

(g) The issue of years of life lost deserves more rigorous discussion and especially the extent to which the reported signal is a sub-set of years of life lost for the smoking population.

(h) The discussion of heterogeneity of response deserves more comprehensive discussion. In my opinion, this includes recognition that the “weak” and variable signal in the NMMAP’s study may be a reflection of heterogeneity. In my opinion, the lack of statistically significant PM associations with increased health risks in all but two cities is a strong argument for thresholds.

(i) The chapter does not adequately discuss the issue of what is the appropriate “exposure metric” for the chronic studies including the ACS cohort and the Six Cities study. More recognition should be given to the possibility that a significant portion of the “signal” may be attributed to early life exposures that undoubtedly were substantially higher than ambient concentrations in recent decades. It is obvious that the larger the appropriate exposure metric, the smaller the risk coefficient.

(j) The chapter’s discussion of exposure-response models that are alternatives to the linear response model is totally inadequate. The issue of the shape of the exposure-response curve at levels in the range of the current PM standard is vitally important to making decisions on the level and statistical form of any future PM NAAQSs.

(k) The chapter should do a better job of presenting data in the PM10 metric. The CD is a science document and its contents should not be unduly influenced by some individual’s views as to interpretations of the Court’s decision on PM excluding consideration of a PM10 metric. The CD needs to be candid in relating the strength of the science basis for PM10, the modest evidence for PM2.5 and the very limited evidence for PM10-2.5.

(l) As the chapter is revised special care should be given to excellent review comments offered by the “public.” Past comments in some cases appear to have been ignored.

(m) The present version gives too much attention to the earlier flawed GAMs analyses and inappropriately uses the earlier flawed analyses to prop up the very “weak signals” for PM effects found when the GAMs analyses were done with appropriate convergence criteria. The flawed analyses have no standing.

(n) Serious consideration in future documents should be given to reporting exposure-response relations if they are linear over some range as increased response per : g/m³ of a particular PM indicator. The use of arbitrary normalization to per 10 : g/m³, 25 : g/m³, etc. serves no useful purpose. I suspect some individuals are concerned that the use of a simple metric – increased response per : g/m³ - will lead the uninformed to think the response signal for increased PM is very, very weak.

Dr. Gunter Oberdorster

REVIEW OF PM HEALTH CRITERIA DOCUMENT CHAPTER 6 – DOSIMETRY OF PM

With the addition of sections on modeling, particle deposition and disposition in the respiratory tract and adding a more detailed discussion on the hot spots, this chapter has been significantly expanded. This expansion raised some additional questions, which are summarized as minor and major comments to be considered in the final version of this document.

Page 1, line 6: I suggest to delete “delivered to” and replace with “at”. A dose may be delivered to the alveolar region, but only when deposited it will actually be able to act at the target site.

Page 9, Figure legend: Add to the end of the legend “and geometric or diffusion equivalent diameter for $<0.5 : \mu\text{m}$ ”.

Page 13, Figure 6-4: This figure from 1989 should be updated with newer data, for example including figures provided in Cheng *et al.* (1996) and by Kesavanathan and Swift, 1998, showing nasal deposition in humans. Also, the figures on deposition from the 1989 Schlesinger publication — although showing nicely the variability of deposition efficiencies between different measurements and individuals — could be updated by a figure summarizing our present understanding of deposition efficiencies in the human respiratory tract, for example, as provided by the ICRP model. It should then be emphasized that there is all that there can be relatively large inter-individual variabilities.

Page 14, lines 21, 26 and 28: Nasal deposition *in vivo* and model studies with ultrafine particles are cited here, and are described as showing consistent results. However, deposition efficiency in the human *in vivo* studies is much higher for the smallest ultrafine particles compared to the model studies. Also, studies by Cheng *et al.* (*Aerosol Science & Technology* **125**: 274-291, 1996) should be included here since these are also studies in human volunteers on nasal deposition.

Page 15, line 1: The nasal filtration efficiency for ultrafine particles applies not to all sizes, only to the smaller particles within the ultrafine range.

Line 18: The same comment applies to this sentence, nasal passages are not an efficient filter for all ultrafine particles $<0.1 : \mu\text{m}$. It is only for the smaller size range. Also, the term “nano” particles is introduced here for the first and only time, and it should be replaced by the term used throughout the document, *i.e.*, ultrafine particles.

Page 16: The text needs to be changed for both figures, the upper figure does not have particles $<0.5 : \mu\text{m}$ and $0.05 : \mu\text{m}$ needs to be changed to $0.5 : \mu\text{m}$.

Pages 17 and 19, studies by Brody and Warheit: Add the sizes of the particles that were used in these studies, *i.e.*, Mt. Saint Helen's dust and carbonyl iron particles.

Page 22, line 1: Change 0.4 to 0.04.

Page 24, line 16: Add "initially" before "inspired ultrafine particle", and replace "in the" with "to grow to a"

Page 39, Figure 10, subfigure D: 70% alveolar deposition for 3 : m particles looks extremely high, is this correct?

Page 43, line 1: Since the title selected for this chapter is clearance and translocation, there needs to be a clear definition for the two terms. As it stands now, in many sections of the following paragraphs translocation is used as part of the clearance mechanisms and *vice versa*. If translocation is used to describe the movement of particles out of the respiratory tract into extrapulmonary organs including the blood circulation, then the generally referred to mucociliary clearance should also be termed translocation. So what is the definition of translocation *vs.* clearance?

Line 12: The categorization of clearance mechanisms into absorptive and non-absorptive is a bit unusual, I suggest to change that into chemical and physical processes.

Page 44, Table 6-2: Again, the title containing both terms clearance and translocation may need to be changed. With respect to the extrathoracic region, several past studies have demonstrated a neuronal pathway *via* the olfactory nerve of soluble metal compounds (cadmium, mercury, manganese, lead, and others) being transported from the nasal olfactory mucosa into the olfactory bulb of the CNS (studies by Tjälve, Dorman, and others). This pathway exists also for solid particles as shown with intranasal instillation studies of colloidal gold and virus particles in monkeys from 1941 and 1971. Most recently we showed this also for inhaled solid elemental carbon particles, however, these results are only published as abstracts and the full paper is under review now and probably cannot be cited.

Page 45, Figure 6-12: I suggest to mark with a question mark the clearance pathways which have not been confirmed in experimental studies (note that the term "clearance" is again used here although translocation pathways are depicted). The questionable pathways would be: Interstitial macrophages passing into the circulation; interstitial macrophages passing through the alveolar epithelium with particles; and particles passing from the interstitium to the bronchiolar and bronchial lumen.

Page 46, line 24: This is one of the hypothetical unconfirmed clearance pathways into the blood stream, *i.e.*, particle-laden macrophages entering the blood circulation. This has not been demonstrated.

Lines 25-30: All of these pathways are most likely size-dependent, that is they are more likely for smaller particles (<0.5 – 1 : m) than larger ones.

Page 47, line 7: Replace “matter” with “mass”.

Lines 19-22: Also mentioned here should be binding of dissolved materials to proteins, receptors or specific molecules.

Page 50, line 15: Add “long-term” in front of “particle retention”.

Page 51, line 30: Cited here is the study by Kreyling *et al.* (2002) on the translocation of ultrafine iridium particles deposited by intratracheal inhalation in anesthetized rats. In the same issue of this journal our study on translocation of inhaled ultrafine elemental carbon particles to the liver was also published and could be cited here as well.

Page 52, line 25: Only 3 : m particles were translocated, 9 and 15 : m-size particles were not in the study by Snipes and Clem.

Page 53, lines 18-30: A cautionary note may be appropriate here to indicate that the stability of the ^{99m}Tc label of the ultrafine particles could pose a problem in the interpretation of the study.

Page 54, line 7: This sentence starting with “This study also indicates ...” should be deleted since the same clearance pattern was found for soluble silver particles as explained in the subsequent sentences.

Page 57, top para.: Another group to be included here are smokers with impaired tracheal-bronchial clearance as reported in several earlier studies.

Page 58, lines 6-11: Included here again can be smokers with several studies showing impaired alveolar macrophage-mediated clearance compared to non-smokers.

Line 31: Tran *et al.* did indicate particle surface area rather than the volume or mass to be the decisive parameter for overload-related effects.

Page 63, line 13: I assume “in vitro studies” was meant to be “instillation studies”? Otherwise, which normal defense mechanisms *in vitro* will be overwhelmed?

Page 64, line 21 thru Page 65, line 30: This section deals with the important issue of hot spots occurring during normal inhalation of particles at carinal ridges. Publications by Balashazy and Hofmann specifically are discussed here. When the high concentrating factors of 600 to 4000-fold surface concentration in hot spots compared to average surface deposition are discussed, it needs to be kept in mind that this is calculated for small patches of 100 x 100 : m, *i.e.*, about 100 cells. If the patch size becomes greater there is a rapid decrease of these concentrating factors. So it should be added that these high local PM doses apply only to very small groups of cells. A newer publication by these authors (2003) makes this more clear. When I talked to Hofmann these hot spots comprise ~1% of the total surface of an airway generation. He also said that these hot spots are more sharply defined for larger particles and become less defined and more diffused for

submicron particles, and there is a rapid decrease of the concentration in the areas next to the hot spots. Also, there is a decrease of the mass depositing in these hot spots the further down towards the respiratory bronchi the particles travel: If, for example, a relative mass of 1000 is deposited in the upper generational carina, then in the generation 15 it is only a mass of 50. Of course, total mass in that area is more because of the high number of carinas present.

The calculation performed on page 65 for an ambient particle concentration of 65 : g/m³ needs to consider these issues. Specifically, since only 1% of the tracheobronchial surface is dosed with these high concentrations, one needs to be careful to assume that in a rat instillation study a dose of 150 : g would be reasonable. It should be at least a factor of 10 less since the assumption in the document is that 10% of the TB area would be dosed by instillation. Furthermore, instillation will induce its own hot spots, and in addition one needs to consider as well the extremely high dose rate in an instillation study vs. the much lower dose rate by inhalation (bolus effect). Thus, these calculation need to be revised or deleted so it is not misused as justification for high dose instillation in rats. Certainly, a cautionary note needs to be added, also considering newer developments with computational fluid dynamics (CFD) which is a very promising tool with respect to microdosimetry as discussed later on page 76 at the end following in this document.

Page 66, line 4: I recommend to replace “useful” with “mandatory”.

Line 8: The term “disposition” is used here to encompass all of the behavior of particles from inhalation, deposition clearance, and retention. I suggest to add to this title “Modeling the deposition and disposition of particles ...” I think that this is a very useful chapter describing the different possibilities available to perform dosimetric analysis, computations and extrapolations for PM studies.

Page 71, line 21: I suggest to add that lung deposits may also be expressed on the basis of per square centimeter of airway surface which will be discussed later in the document.

Page 75, lines 12-28: The differences in rodent vs. primate lungs in terms of particle retention in the interstitium vs. airway lumen are discussed here. As I had commented in a previous version of this document, the interpretation of the findings of differences between interstitial burdens in these two species is not as straightforward as it appears, given that there is no information of the lymph nodal burden in the studies. We know that in general clearance in rodents is faster than in primates (for example, pulmonary retention halftimes in rats of ~70 days vs. 400-700 days in humans), and although we don’t know about the interstitial clearance rates we know that in an overload situation there is significant accumulation in local lymph nodes, and given that the rat studies were examined towards the end of their lifespan the interstitium may have been cleared much more efficiently by that time than in primates which gives the appearance of differences in clearance pathways. This point ought to be addressed here.

Page 82, lines 4-18: It would be helpful to include the particle sizes modeled in these studies using CFD.

Line 25: The MPPD model (one of the two mentioned here) can model any density, not just unit density.

Page 88, lines 1-22: When describing general characteristics of the MPPD model, it should also be mentioned that the dispersity, inhalability, particle density, respiratory pause, and surface area doses and other parameters can be modeled and calculated.

General comment – In this context of different dose parameters I suggest to consider a short section on Dosimetry, Particle Parameters and Mechanisms. In this added section the importance of mass dose *vs.* surface area dose could be discussed, *i.e.*, dose expressed as deposited mass per lung surface area, *vs.* mass per g of lung. These different dosemetrics imply different mechanisms with respect to effects, that is, particles interacting with airway epithelial cells, with interstitial cells; and includes also aspects of solubility since soluble components by diffusion may target a number of different cells whereas insoluble particles may interact primarily with alveolar macrophages and epithelial cells, but also depending on their size translocate to interstitial and extrapulmonary sites. A further step is to include particle surface area as another dosemetric, particle surface area per g of lung *vs.* particle surface area per lung surface area.

Different endpoints and different mechanistic pathways are implied by how the dosimetry of particles is described and expressed, for example, for lung tumors airway epithelial cells are the target cells whereas for other effects interstitial cells may be targeted. Thus, when extrapolating from results of animal studies human exposure concentrations extrapolated on a lung weight basis will be different than those extrapolated based on the lung surface area, and these differences can be quite significant. This is also borne out by the figures shown in this chapter when particle deposition is modeled with the MPPD model either on a per g lung basis or per cm² surface basis, there are some similarities but also significant differences as stated on page 101. In addition there is the issue of default values as commented upon further below. Thus, a brief discussion of these dosimetric issues for extrapolation of effects and correlation with mechanisms might be helpful here.

Page 92, Table 6-5: This table is for the 3-year old human, and FRC that is lower than the FRC for the younger age group. This seems to be a mistake?

Page 96, lines 11 and 12: Replace “in²” with “m²”. The value of 9.35 m² given in line 12 is different from 7.3 m² in Table 6-7 on page 100. Are these for different lung regions, what is pulmonary 2 region? If it is respiratory bronchioles, then use that term instead of pulmonary 2 region and use the same number.

Line 33: Explain why the model for humans assumed light exercise, *i.e.*, a tidal volume of 1250 mL at a breathing frequency of 20 respirations/min., whereas for rats resting conditions were used. Also, make sure that in the following figures in this section the legends indicate that light exercise was modeled in humans.

Page 100, Table 6-7: One problem with modeling obviously is that there are several “default” values which differ substantially. For example, this table lists the surface area for the human lung

either as 54 m² or 150 m², quite a difference. Likewise, the surface area for the tracheobronchial region on page 65 of this document was given as 0.247 m² for humans and as 0.0027 m² for rats which is closer to the EPA default value but different from the MPPD model. It would be worthwhile to address this issue in a short paragraph, pointing out that there is a need for agreeing on a “normal” value for respiratory parameters and anatomical data.

Page 102, line 6: As commented before, translocation is used here in addition to clearance, and if that is clearly defined at the beginning that would be OK. On the other hand, if translocation is part of the clearance that ought to be changed here.

Lines 13 and 14: Before the word “ultrafine” the word “smallest” should be included, and before the word “coarse” the word “larger” should be added. For these smallest uf and larger coarse particle sizes the nose is actually very efficient and not a moderately efficient filter. In lines 17 and 19, it is stated that deposition patterns for ultrafines and coarse particles are similar which is reasonably true, but it would also be worthwhile to include a statement here that within the ultrafine particle range and within the coarse mode particle range there are significant differences with respect to their deposition efficiencies within the three regions of the respiratory tract; for example, the smallest of the ultrafine particles have a very high deposition efficiency in the nose, sizes around 5 : m to 10 : m have high deposition efficiencies in the tracheobronchial region and sizes around 20 nm have very high deposition efficiencies in the alveolar region, and similar statements can be made for coarse particles as well.

Lines 26 and following: As discussed in the main text (page 26), the gender differences that were found are only slight which ought to be indicated here too.

Page 105, paragraphs starting on line 6: Again, the difference between clearance and translocation ought to be considered, I favor translocation being part of clearance which means that the sentence as stated in the third line of this paragraph would be OK.

CASAC – REVIEW OF CHAPTER 7, TOXICOLOGY OF PM

Page 1, line 9: Delete “evidence is available for elucidating” and replace with “are”

Page 5, line 21: It is stated here that doses administered by instillation are accurate; however, this is a general misconception, a certain amount instilled will not at 100% be in the lower respiratory tract, most of the time there is some coughing-up such that the retained dose immediately determined after instillation is between 80-90% only. So the term “accurate” may be replaced with “is better defined”.

Page 5, line 31 and Page 15, line 1: The levels of ultrafine particles delivered as polymer fume was actually low, 20-50 : g/m³ expressed as mass; of course, the number concentration is very high.

Page 13, Table 7-3: The studies by Elder *et al.* (2000a, b) should also be listed here in the table of surrogate particles given to laboratory animals. These studies are cited later under a different

category, but ought to be included here as well. Also, in this table, the term “clearance halftime” is used, this should be replaced by “retention halftime”.

Page 17, line 29: How much greater was the metal content when the plant was open? It would be helpful to indicate this in terms of fold-increase or percent of extract.

Page 19, lines 11 and 12: This is one of several examples showing that intratracheal instillation results in greater acute responses compared to inhalation and it would be useful to add a respective note here to point out this important difference.

Page 23, line 28 to Page 25, line 29: I suggest to delete this section since these are older studies from an earlier PM Criteria Document described here. They also are placed here in a section dealing with human studies, both before and after the description of these older studies. Instead, I suggest to move the summarizing paragraph of this study, page 25, lines 30- page 26, line 15, to the end on page 27, line 23.

Page 37, line 6: The conclusion that high metal content of all fly ash can alter epithelial cell barrier is not obvious from the study as described here. Did the authors use a metal chelator as a control to justify this conclusion?

Line 22 – 29: The studies by Elder *et al.* (2000a, b) are listed in the accompanying Table 7-6, but not described in the text. These could briefly be summarized by stating that priming of the respiratory tract by inhaled endotoxin increased the effect of inhaled ultrafine surrogate particles and ozone.

Page 47, lines 12, 13: 15 mg/m³ do not closely mimic environmental exposures, this needs to be changed.

Page 52, lines 1-8: The main finding of this study by Nemmar *et al.* is that electrical charge makes a big difference in that only positively charged ultrafine particles resulted in thrombus formation.

Page 62, Section 7.4.2.1, ambient particles: A number of these *in vitro* studies have already been described in this Chapter 7 before. Why are they described again here?

Page 67, line 22: Reference is made here to a “non-cytotoxic level of ROFA”. This may infer that low doses have been administered, however, cytotoxicity is not a measure of relevant doses. 200 : g/mL in this case is pretty high.

Page 68, lines 11-14: The summary that ROFA exposures increase oxidative stress, *etc.*, needs again the qualifier that this is seen at high doses.

Page 80, lines 23 – Page 81, line 4: Since no control particle was given in this study, a caveat ought to be included that any high dose particle may cause the same effects.

Page 82, line 9: What are “visible” particles?

Page 85, lines 1-5: The surface area concept for PM toxicity is described here and the question is raised as to whether other endpoints can confirm this concept. There are a number of other studies with different endpoints, indeed, showing that particle surface area is a better dose-metric than particle mass; for example, Driscoll *et al.* summarized a number of long-term inhalation studies in rats with poorly soluble particles of low cytotoxicity with respect to a correlation of different particle parameters and the endpoint lung cancer and found particle surface area to be the best fitting dose-metric.

Line 15: Penetration of ultrafine particles into the airway epithelium is addressed here, however, that this is particularly significant for ultrafine droplets is not very meaningful for this mechanism; droplets lose their particulate state immediately upon deposition on the airways. So, what is the intent of this sentence?

Pages 96 – 99: A number of studies with findings on immune responses and allergenic sensitization using diesel particulate matter (DPM) are described here. One of the studies (and there are newer ones presented at this year’s AAAR meeting) showed that carbon black resulted in the same immune responses as DPM, indicating that a particulate compound per se and not necessarily ambient PM alone can induce these changes. It needs to be pointed out, therefore, that in almost all of the DPM studies listed here, no control particle has been administered at the same time for comparison. Using DPM alone is insufficient, in that case one will always arrive at the conclusion that DPM is allergenic once a high enough dose is used to get a response. However, if such response is due to a general generic particle effect, then DPM would be one of many compounds being able to cause these responses. Focusing on DPM gives the impression that DPM is particularly active in this regard.

Page 103, line 17: Replace “many” with “most”

Page 110, line 18: Add before “carbon” the terms “singlet ultrafine”

Page 117, lines 3/4: As mentioned above, with respect to the allergenic responses of diesel particulate matter it needs to be pointed out that carbon black particles can be as effective and that diesel should not be singled out as the most active particle type for such responses. The emphasis on DPM in connection with allergic responses is repeatedly made in this summary. For example, on the same page, line 11, DPM is referred to as being unique with respect to its adjuvant-like activity; however, what is missing is to point out a lack of studies with a comparison particle such as carbon black, and the few that are out there show that DPM, indeed, does not seem to be as unique.

Page 120, line 4: The mechanism may not only be highly dependent on the type of particle but also on the dose which ought to be added here.

Page 121, lines 1-9: A comment to the dosimetry of the well-conducted human instillation study with Utah valley dust before, during and after closing of the steel mill: Using the MPPD model and a particle size of 1-4 : m, the instilled dose of 500 : g is about 20 times higher compared to a 24-hour inhalation at 100 : g/m³ and 15 L minute ventilation. Only ultrafine particles (20-50 nm) have deposition efficiencies of 30 and more percent resulting in about 7-fold overdosing compared to inhalation.

Line 22: ROFA causes the substantial effects only at high doses/concentrations.

Page 122, lines 1-20: Two studies are listed here on increased susceptibility to respiratory infections: both use again very high doses or concentrations which needs to be pointed out.

Lines 23-31: Again, the DPM and allergic responses are addressed here, and again it is ignored here that carbon black has been shown to be as effective. In fact, at this year's AAAR meeting in Pittsburgh, studies from Holland have shown that DPM was less effective among several dusts tested for their allergic responses in rodents.

Page 127, line 17-22: Again, the same comment applies to this section describing DPM allergic responses, neglecting the lack of control particles used in these studies.

Dr. Robert D. Rowe

Memorandum

To: Phil Hopke, Fred Butterfield
From: Robert Rowe, Stratus Consulting, Stratus Consulting Inc.
Date: 8/18/03
Subject: Initial comments on June, 2003 Draft of PM CD

As requested, by comments focus on the welfare effects presentations in Chapter 4 and the related material in the Executive Summary and Chapter 9. Limited economics materials remain in the CD for me to comment on.

Where specific edits are suggested to existing text, recommended deleted text is noted by ~~strike through~~ and recommended additions by underlining.

Chapter 4 – Welfare Effects

The revised presentations (here and in other chapters) addresses several of the September 30, 2003 recommendations and is improved, but overall could continue to be improved to be more consistent with the other chapters in terms of clearly providing information to address risks of PM exposure at or near ambient levels (CASAC letter of September 6, 2002 page 6).

Title. It makes sense to me to change the title of this section from “Environmental Effects...” to “Welfare Effects...” to be consistent with the “welfare effects” orientation of the secondary standard, and that materials damage seems inconsistent with “environmental effects.”

Section 4.2 – Ecosystems

1. The discussion of ecosystem economics was only slightly modified, seeming to miss much of the point of the earlier recommendation. Therefore, I specifically recommend the following edits (retaining some of the citations EPA seems interested in).

- Page 4-57 line 23. Delete the sentence: “Goods have market value; whereas services usually are not considered to have market value.” The sentence is wrong as simplistically presented (many services have market values), is made in a vacuum (re the valuation of goods and services), and the sentence is not needed anyway.

- Page 4-57 lines 26-27 – edit as noted. “~~The majority of t~~These attempts have been controversial because of a lack of agreement on the measurement and philosophical basis for placing a value on ecosystem services.” If desired, EPA could cite Myrick Freeman’s and related papers (and recognize the total versus marginal issue)) after measurement, and cite Heal after philosophical basis. The measurement issue is easily as or more important than the

philosophical issue.

- Page 4-57 Lines 27 – 30. This sentence is not offending, but not particularly helpful for the current policy circumstance. The point Constanza et al is making generally refers to the loss of “total values” for all (or portions of all) ecosystem services, whereas the relevant economic analysis for PM standard setting is for marginal changes in ecosystem goods and services due to varying levels of air pollution impacts, which generally is not the total loss of some services.

- Page 4-57 end of Line 30 through Page 4-59 mid line 16. Delete this entirely. It serves no purpose to the current document. Why does EPA persist in presenting a discussion between ecologists and economists that is inconsistent with the use of economics to value marginal impacts, as called for under the criteria for setting secondary standards (consideration of, but not sole determination by, economic information).

- Page 4-58, line 16 through line 26. This is all well and good, but why it is placed here?

2. Section 4.2 remains a compendium of information for which it remains difficult to ascertain which information is relevant, in general and in particular, for setting secondary PM standards. The Chapter and section introductions focus on vegetation with little attention to the full range of possible ecosystem impacts (aquatic quality and life, terrestrial animals,...). As previously noted, it seems appropriate to identify the full spectrum of possible impacts and indicate why the focus is on terrestrial vegetation.

3. Minor edits

- Figure 4-2 page 4-11. Please label the two parts of the figure and the y axes.

- Page 4-64 (and elsewhere), discusses salinity through sea spray, as opposed to salinity from road salts and cooling towers – is this length useful as we will not regulate sea spray.

- page 4-75 at top. It may be useful to cite the EPA Mercury documents.

- Page 4-94 bottom. Could some indication be presented as to the concentration levels (or haze levels) that are presented for China as “especially severe”? This paragraph would be more useful if we knew if the levels were a couple times, or 10-20 times what is experienced in the U.S.

Section 4.3 Visibility

1. Section 4.3.7. This might be better titled “Welfare Impacts of.... “ or “Societal Impacts of...” Then, one could also make reference to perception and attitude studies that indicate that visibility impairment consistent with current levels of particulate matter are both perceived by individuals, and often considered to be adverse (economic studies include this through WTP to

reduce visibility impacts and relationships between visibility and property value declines, as do perception and attitude studies such as the Denver/Ely study, which can be cited). A couple paragraphs and/or citations would be most useful.

Section 4.4 Materials...

1. Perhaps it is useful to more explicitly state/conclude that there are limited new studies on the societal/economic impact of PM on materials since the 1996 CD and Staff Paper.

Chapter 1. Introduction

1. Minor edits.

- Page 1-3 Line 14. “The last ~~previous~~ review of...” (redundant).
- Page 1-13 line 2 “from the most recent ~~previous~~ PM, Ozone,... efforts.”

Executive Summary

1. Introduction and Health Section – minor edits.

- E-9 Line 2. Add “in” “in many urban areas.”
- E-11 line 3 at end add “ambient” -- daily ambient PM....
- E-13 item 31 line 8, edit “~~is~~ maybe transferred” to keep the tone consistent.
- E-17 item 5. Line 1 (CAPS) to (CAP). Line 3 edit: CAP studies ~~used~~ collected
- E-21 item 9 is unusually vague. In several places here and subsequent pages “which” perhaps should be “that”. Item 11 “evaluate the effects of combinations...”
- E-22 Item 7 line 6 remove un in ~~unusually~~ Item 8 line 1 “... ~~a number of~~ more than (≥ 35) ~~of~~ important PM....”
- E-25 Item 11 line 6 “emerging new” seems redundant.
- E-27 item 1 last sentence. “..... data quality or representativeness, are intrinsically likely to be less credible reliable and should ~~not~~, in general, be used ~~without~~ only with careful assessment....

2. Welfare effects sections

- E-29. Consider title change from “Environmental Effects...” to “Welfare Effects...”
- Section E.6.2 (page E-35) - Visibility. Another bullet could be added to the effect of “Human perception and economic studies demonstrate that the public consider the existing chronic and episodic visibility impairment related to PM at many locations to be adverse (reduces individual’s welfare).” See comment under Chapter 4, Section 4.3.
- Section E6.3 Materials... Consider comment about limited new studies on societal impacts (see suggestion under Section 4.4 above).
- Section E.6.1 (Vegetation/Ecosystem) The tenor is a bit different than for the other sections of the Executive Summary (particularly bullets 1 and 2 -- “Human existence on this planet depends on ...”, “..human activities are creating disturbances...”, which are generic statements that are not at issue and similar statements are true of air quality for humans to breathe, but EPA doesn’t make that presentation in the health sections in favor of more specific content). The remaining points presented are consistent with Chapter 4.2, but some could be more specific to the PM standard setting or more explicit in their point. A few from the chapter to consider include:
 - A The relationship between ambient PM concentrations and ecologic impacts is less well understood and specified than for human health, in part because of the tremendous diversity and complexity of ecosystem resources and their response to air pollution.
 - A PM effects on vegetation are more related to the chemical constitution than to the PM size classes (p 4-5, 19).
 - A Experimental applications of PM constituents to foliage typically elicit little response at the more common ambient concentrations (page 4-60 line 24), while significant effects are observed at elevated concentrations of many constituents (including metals,) near point sources (found throughout the document).
 - A The vegetation effects of exposure to PM vary widely depending on the concentration and composition, site characteristics (terrain, deposition mode, meteorology) and the vegetation characteristics. Thus, the impacts of the same concentrations may vary dramatically from site to site from no impact to impacts on individual plants, populations impacts and to ecosystems impacts. In many, if not most, cases, the specific impacts have not been thoroughly studied, nor translated to an ambient concentration- response relationships.
 - A Although forest ecosystems other than the high-elevation spruce-fir forests are not currently manifesting symptoms of injury directly attributable to acid deposition, less sensitive forests throughout the United States are experiencing gradual losses of base cation nutrients, which in many cases will reduce the quality of forest nutrition over the long term. (page 4-115). Acidic deposition is having a significant effect on nutrient cycling in most of the forest ecosystems studied in the IFS project. (page 4-136).

Chapter 9 (Welfare effects sections only)

1. Introduction. A few edits to the introduction could make it a bit cleaner in terms of separating materials for the primary and second standard. E.g.,

- Page 9-1, lines 5-7. “This chapter first focuses onin the United States, as is the focus of the primary standard. As such, ~~the chapter~~ Sections 9.2 through 9.9 updates the integrated.....” (Same for Page 9-4 lines 6-7)

- Page 9-1, line 11. “~~It also~~ Section 9.10 highlights key findings on environmental welfare effects of airborne PM, relevant to the secondary standard.”

- Page 9-4 line 11. The size distinction is of particular relevance to the primary standard (edit to make clear this discussions is particularly relevant to the health/primary standard.

- * The PM size class is also likely important to materials soiling and visibility and should be so stated somewhere (Chapter 4 and here), but the vegetation discussions make a point that this distinction is not necessarily fundamental to these effects (other than perhaps through deposition).

- Page 9-5, lines 23-26. Separate paragraph. Edit from “environmental effects” to “Welfare effects” and “at the end of this chapter” to “Section 9.10”.

2. Welfare Effects

- Page 9-139, line 20. Delete “concise,” which is subjective and not needed.

- The comments on this material in Chapter 4 and the Executive Summary apply equally here. In short:

A An appropriate title may be “Welfare Effects”.

A The conclusions regarding visibility (it is adverse at current levels) and materials (limited work since 1996) could be augmented. The climate change conclusions are clear – there is great uncertainty.

A The vegetation/ecologic effects section could be shortened to be more to the point by: reducing generic discussion of the importance of ecosystems and of the organizational structure, reducing lesser points in favor of highlighting specific conclusions that may (or may not) support the stated goal of evaluating “possible revisions to the PM secondary standards to protect against PM-related welfare effects.” (page 9-4 lines 1-2), including concisely stating key unknowns and uncertainties.

Dr. Jonathan M. Samet

Review Comments: Air Quality Criteria for Particulate Matter (Fourth External Draft)

Chapter 8: “Epidemiology of Human Health Effects Associated With Ambient Particulate Matter”

Prepared by: Jonathan M. Samet, M.D., M.S.
Professor and Chairman, Department of Epidemiology
Johns Hopkins University Bloomberg School of Public Health

In general, this chapter is improved from earlier versions, even though substantial updating has been needed following reanalysis of major epidemiological studies because of statistical issues. The structure is clear and appropriate, the text emphasizes the principal, relevant studies, and an effort is made to synthesize and interpret the evidence. The efforts to interpret the findings represent a substantial advance over the prior versions. In general, conclusions appropriately reflect the advances in knowledge since the 1996 Criteria Document.

The chapter covers a massive body of evidence and there are minor problems in the details. However, I offer only the following general remarks for consideration:

- Because of the scrutiny brought to bear on the time-series results following the identification of a statistical software issue, model fitting has been discussed extensively. The Criteria Document reflects this scrutiny and attention to model details in its text. However, the mistaken impression could be gained from the text that there is a “correct” model, which remains elusive to investigators. This is not the case, and models can only reflect the state of knowledge. The robustness of findings to reasonable sensitivity analyses is more relevant and deserves emphasis. Text surrounding model fitting should be reexamined with this comment in mind.
- There is substantial discussion of “confounding” and “effect modification” by other pollutants, in assessing the effects of PM. The proposal that the co-pollutants may be confounding is based in one formulation of how the multiple pollutants within the complex mixture of urban air may exert their action. Whether the effects are independent, however, is uncertain and the text could do a better job of placing findings on PM within the broader formulation of urban air as a complex mixture.
- As data are available, the text discusses components and characteristics of PM that may determine toxicity. This is a difficult area for interpretation and consideration should be given to the appropriate criteria for inferring that one or another component is particularly toxic biologically.
- The text discusses “interventions”, referring to examples of “natural experiments” in which step changes in PM concentrations have occurred. These studies are not interventions in the experimental sense, but rather represent examples of “found experiments”. The advantage of

such changes in exposure is the decoupling of change in exposure from factors that might be confounding its effect. There is an opportunity to strengthen causal inference as a result.

- In presenting the sweep of the evidence, there is a tendency to be insufficiently critical and to not give weight to the various studies based on qualitative considerations, at the least, of quality. This is evident, for example, in the discussion of the prospective cohort studies.

Chapter 9: “Integrative Synthesis”

At the last review, I found this chapter to be less a “synthesis” than a “summary”, and recommended a structure that might build from the source-to-effect framework proposed by the National Research Council’s Committee on Research Priorities for Airborne Particulate Matter. That framework has now been incorporated and synthesis is attempted in relation to some aspects of the epidemiological findings. However, in general, the chapter still fails as a “synthesis”. Rather, it provides summaries of already introduced material and in places, it reads as a primer. This is not the location, for example, to be covering basic aspects of particle size distribution and lung symmetry.

What might be expected from a chapter intended to be a “integrative synthesis”? Given the suggestion of using the NRC’s Committee’s framework, the synthesis should be built around this conceptual model. At the end of the discussion, there should be consideration as to the confidence with which sources can be linked to health effects, building from the certainty with which the arrows linking the boxes within the model can be assumed as correct representations. Some portions of the current chapter are on-target with this approach, but most are not. At its end, the chapter might return to the current standards, in anticipation of the “Staff Paper”, at least summarizing what has been learned that would be relevant to any change in the elements of the PM standard.

Thus, I would urge a redrafting of the closing chapter. It needs to be much shorter and the text that is simply repeated from earlier chapters should be removed. The chapter appears to be multi-authored; perhaps it would benefit if a single author were to have the task of writing a more unifying document.

In addition to this overall, general concern, I have a number of specific methodological/ conceptual issues that should be addressed during the redrafting:

- As I noted in regard to Chapter 8, the authors of the Criteria Document have failed to adequately represent the issue of PM as a component of the air pollution mixture. Consequently, there is a diffuse, and conceptually blurred discussion of issues around PM as a mixture component. Discussions of confounding, effect modification, and “mixtures”, along with considerations of sources, reflect varying views of PM and its effects on health in relation to other pollutants. Consequently, text on the independence of PM effects is rather murky.
- I found the discussion of exposure to be particularly weak in many respects. An adequate

foundation is not built for interpreting the epidemiological studies, and complex matters around exposure error, model building, and “surrogate pollutants” are blurred. The authors do not recognize that longitudinal correlation between personal and ambient concentrations is relevant to interpretation of the time-series studies. Issues around measurement error and mixtures are presented with a view that they cannot be resolved, which will inevitably cloud interpretation of the epidemiological findings.

- The chapter reads as though little is known about “mechanisms”, in spite of decades of research on how particles may affect the lung and other organs. This work cannot be characterized as in its “early” stages.
- The issue of causal interpretation of associations is dealt with only by indirect reference and in places causality is mentioned in quotation marks, without explanation. This chapter should offer a stronger view in terms of the interpretation of the collective body of evidence around causality of effects. Since 1996, hasn’t the evidence strengthened the case for causality and shifted consideration to the dose-response relationship, critical sources, and susceptible populations?
- The chapter provides a scattered discussion of issues related to characteristics of particulate matter that may determine toxicity. Much of this discussion is weak, reflecting the earlier failure to establish a clear framework for considering this difficult problem.

Additionally, I have the following specific comments:

- Page 9-4, line 26: “valid” is equivalent to “causal”?
- Page 9-50, line 29: “correlation” should be replaced by “association”.
- Page 9-52, lines 8-10: This sentence is not a correct representation of the views of the National Research Council’s Committee and should be corrected.
- Page 9-66, lines 1-4: This is an inadequate summary of an important literature.
- Page 9-67, line 21: See earlier comment concerning work on mechanisms.
- Page 9-67, lines 29-30: Here, the impression is given that there may be “specific causal agents”.
- Page 9-70, lines 1-15: These sentences simplify the conceptual ambiguity of much of the interpretation offered in this chapter.
- Page 9-73, lines 23-29: Again, too sweeping and lacking clarity.

- Pages 9-112, 9-113: This text illustrates the weakness of the chapter and the Criteria Document in dealing with the multi-pollutant issue.
- Page 9-115, lines 15-18: Of course, more models can be fit to any dataset, but the analysis by Daniels et al., shows little evidence for departure from linearity. In fact, a remarkably strong dataset would be needed to test specific alternatives. This text is unnecessarily general in its criticism, without offering any reasonable alternative approaches.
- Page 9-116, lines 23-27: The “PM exposure paradox” represents a failure of the document to correctly address measurement error structure relevant to interpreting the time-series models.
- Pages 9-127—9-129: The word “coherence” is used often and with different intent throughout the document. This section finds the epidemiological evidence to be “coherent” without any discussion as to the criteria for gauging coherence. Elsewhere in the document and in other contexts, coherence has been used more broadly to refer to the meshing of different lines of evidence in producing a cohesive scientific story. A discussion of coherence, with this in mind, is needed in this chapter. These pages are weak and simply say that the authors find the evidence to be coherent without saying much more.

Dr. Warren H. White

Visibility Warren White, 8/20/03 all references given as page/line

The treatment of visibility in PMCD draft IV remains unsatisfactory. The theoretical relationship of visibility to PM concentrations is systematically obscured and the observed relationship is discounted. Even as discussion is avoided on the straightforward dependence of haze on PM_{2.5}, haze is quantitatively attributed to individual chemical species. These attributions are so garbled as to be meaningless.

Consider what the busy decision-maker learns about visibility from the thirteen bullets in the Executive Summary.

E-35/8 The first bullet is a wonderful distillation of the state of present understanding.

E-35/9 The second bullet talks about what we mean by visibility. It's appropriate.

E-35/10 The next four bullets give a tutorial on atmospheric optics, going well beyond
to E-36/2 what a reader needs to take away from an ExSumm. At least they are not wrong, although the last of them actively invites the mis-impression that air pollution has a limited role in impairing visibility. "Visibility .. is affected by .. non-air quality related effects [including] .. location of clouds, and reflectivity of the ground. These effects are independent of effects due to changes in atmospheric constituents."

E-36/3 The seventh bullet seems just a less felicitous restatement of the first.

E-36/4-5 The eighth and ninth bullets list measurable indicators of visibility and introduce the deciview as a perceptual metric. It is unclear why purely optical indicators such as contrast transmittance and deciview merit attention in the ExSumm of a PM document.

The first two of the three pages in ExSumm are thus occupied with definitions and introductory generalities. Actual findings come only on the third and last page.

E-37/1-4 The final four bullets review the geographic distribution of haze and its causes. Some of their information is correct and useful, some is not. As will be detailed below, they are largely untethered from the body of the document. As an example, the concluding bullet gives specific findings mentioned nowhere else in the document, taken from a 1999 paper that is missing from the list of references.

And that's it! No mention that the extinction coefficient is proportional to the mass concentration, for a given particle mix. The reader comes to this document familiar from

everyday life with one index of visibility, the visual range, and never learns that this is roughly proportional – in both theory and observation – to the inverse of PM_{2.5}.

In the body of the document, Pages 4-153 through 4-167 are spent on details of human vision and atmospheric optics, most of them superfluous and a few of them wrong. Just one paragraph, on 4-168, finally acknowledges studies showing “a relationship between enclosed nephelometer light scattering measurements and fine particle mass collected on a filter”. It then proceeds immediately to speculate that “the relationship between fine particle mass and light scattering may differ between locations and for different times of the year.” McMurry’s 2000 NARSTO review, cited elsewhere, was more upbeat (*Atmospheric Environment* 34, page 1970): “Although the amount of light that an aerosol with a given mass concentration scatters depends on its size distribution, measurements have shown that the ratio of the dry scattering coefficient to the dry fine particle mass concentration measured at various locations does not vary a great deal.” Strangely, the document seems more comfortable with the use of optical measurements to indicate particle mass than it does with the use of mass measurements to indicate optics: “Trends in visibility impairment or haziness often are used as indicators of trends in fine particles mass.” (4-178/19) “... currently available techniques for continuous measurements of suspended particle mass, e.g., the integrating nephelometer ...” (2-99/6)

Many of the “hard facts” in the Executive Summary, Summary and Key Conclusions (4.6), and Integrative Synthesis (9) take the form of quantitative apportionments. Take, for example, E-37/2 “Organic carbon is the greatest cause of light extinction in the Pacific Northwest, Oregon, Idaho, and Montana, accounting for 40 to 45% of the total extinction.” That’s interesting. And it may be true. Or it may not be, according to the reference apparently underlying all these statements, the 1999 Trends Report (USEPA 2001; page 111): “...sulfates account for over 50 percent of annual average aerosol extinction [at] Mt. Ranier, WA, and Redwood National Park, CA.” Whether true or not, there’s no mention of organic carbon in that specific region anywhere else in the whole document.

The Summary and Key Conclusions (4-236/18) and the Integrative Synthesis (9-151/3) both state that “Nitrates contribute about 45% to the total light extinction in the West ...” and that “Organic carbon is the greatest cause of light extinction in the West, accounting for up to 40% of the total extinction”

This doesn’t make sense even on its face: organic carbon, at “up to 40%” is greater than nitrates, at “about 45%”? The main text (4-179/8) is internally consistent, and shows where the problem is:

“Carbon-based particles are responsible for ... 25 to 40% [of the visibility impairment] in the West. Nitrates ... are responsible for between 5 to 45% of the light extinction in the West.”

But the main text is itself not an accurate account of the 1999 Trends Report (page 111), which appears to be its source:

“Organic carbon typically makes up 25-40 percent of aerosol light extinction in the rural west, elemental carbon (absorption) accounts for about 10 percent....Nitrates typically account for less than 10 percent of total light extinction in western locations, except in the southern California region where it accounts for 30-45 percent.”

So “carbon-based particles” according to the trends report are responsible for 35 to 50% of the extinction. And “5 to 45%” is not a very meaningful description of nitrate’s contribution “in the West.” Meanwhile, the ExSumm (E-37/1,2) steers an independent course:

“Nitrates account for 10 to 20% of the total extinction in other areas [than southern California] of the United States. ... Organic carbon contributes between 15 to 20% to the total extinction in most of the western United States ...”

Similarly, the Summary and Key Conclusions (4-236/15) and the Integrative Synthesis (9-150/31) both state that:

“Up to 86% of the haziness in the eastern United States is caused by atmospheric sulfate. Further West, scattering contributions to visibility impairment decrease to from 25 to 50%.”

The main text (4-179/6) clears up the confusion over scattering in the West:

“In the east, sulfates are responsible for 60 to 86% of the visibility impairment. The sulfate contribution decreases further west but is still responsible for between 25 to 50% of the visibility impairment.”

But both versions of the eastern claim are meaningless, because this document measures “haziness” and “visibility impairment” in terms of deciviews, a nonlinear function of extinction. Stop and consider: according to Figure 4-39a, 1999 visibility impairment in the east was about 21 dv on typical days and 28 dv on the haziest days. According to EPA’s Regional Haze Guidance, “natural” impairment there is around 7.6 and 11.5 dv on typical and haziest days. The natural impairment thus amounts to 36% (typical days) to 41% (haziest days) of the total impairment. What, then, does it mean to say that sulfate causes 86% of the impairment or haziness? The 1999 Trends Report (page 111) shows where the numbers came from:

“... for most rural eastern sites, sulfates account for more than 60 percent of annual average light extinction on the best days and up to 86 percent of annual average light extinction on the haziest days.”

Budgeting makes sense in terms of extinction, but does not in terms of haziness or visibility impairment as the Agency defines these terms. Note, however, that simply replacing “haziness” or “visibility impairment” by “extinction” in the document’s statements still leaves them almost wholly ambiguous. If sulfates cause up to “86% of the extinction in the eastern United States”, what “extinction” does *that* refer to? The average over all days and all sites? The annual for at

least one site? The regional average for at least one day? The highest day observed at any site? These questions of course apply equally well to the attributions for nitrate and carbon. This is an example where the ExSumm (E-37/3) got it right:

“Haziness in the eastern United States is caused primarily by atmospheric sulfate.”

There are plenty more where these came from. Consider organic carbon in the East (emphases added):

4-236/19 “Organic carbon ... [accounts for] up to 18% of the visibility *impairment* in the and 9-151/5 East.”

4-179/8 “*Carbon-based particles* are responsible for 10 to 18% of the visibility *impairment* in the East...”

E-37/2 “Organic carbon contributes ... **20 to 30%** [of the total extinction] in the remaining [outside most of the west] areas of the United States.”

Or elemental carbon in the East:

E-37/3 “Light absorption by carbon is relatively insignificant but is highest in the Pacific Northwest (up to 15%) and in the eastern United States (3%).”

No values for absorption by carbon appear in the body of the text, but the 1999 Trend Report (page 111) gives 10% in the rural West, which is higher than the 3% upper bound implied by the ExSumm and higher than the Trend Report’s value for western nitrate outside southern California.

My point in grinding through the above comparisons is not that any particular number is right or wrong, but that numbers with significant policy implications have been scattered about seemingly for decoration, with little concern for their meaning. In a document that will form the accepted baseline for future documents, that should not be acceptable. And it’s not just the attribution numbers that are capricious: look at Figure 4-39a, and then read the text at 4-180/31:

“In the East, there was a 16% (1.5 deciview) improvement in haziness on the clearest days since 1992.”

This is not some problem of figure reproduction quality, because the 1999 Trend Report (page 105) sees the same figure this way:

“Visibility impairment in 1999 for the clearest 20 percent of days is approximately equal to 1992 levels of 15 deciviews.”

Two other, smaller, points seem policy relevant. The first is that the Summary and Key Conclusions (4-236/2) and the Integrative Synthesis (9-150/18) claim, without qualification, that

“A change of 1 or 2 deciviews is seen as a noticeable change in the appearance of a scene.”

The body (4-167/29) is a little more careful:

“A change of 1 or 2 dv in uniform haze under many viewing conditions will be seen as a small but noticeable change in the appearance of a scene regardless of the initial haze condition.”

The developers of the deciview scale (Pitchford and Malm, 1994) presented no field data of their own, but gave a reasonable argument for the plausibility of 1 or 2 dV as a just noticeable change under ideal field conditions, conditions which include the presence of a natural scenic element at a distance just above or below the visual range. Last year, however, Ron Henry (*JAWMA* 52: 1238-1243, 2002) examined “the only available experimental data taken in the natural environment on the ability of an observer to perceive small, incremental changes in the colorfulness of objects seen through atmospheric haze”. He concluded that “a 1-deciview change never produces a perceptible change in haze,” and that the deciview scale is “not .. uniform over a wide range of visibility conditions, as has been previously claimed.” That critique needs acknowledgment or rebuttal if the statement that 1-2 dV is noticeable is retained in this document.

Finally, the Summary and Key Conclusions (4-236/22) and the Integrative Synthesis (9-151/7) toss a policy “aside” into the otherwise unexceptionable statement that:

“Coarse mass and soil, primarily considered “natural extinction,” is responsible for some of the visibility impairment in the West...”

Does the Agency in fact generally presume suspended coarse particles and fine soil to be natural?

The status of particle-bound water Warren White, 8/22/03 references: page/line

The document’s account of PM measurement rests heavily on the assumption that, as Figure 2-15 puts it,

2-42 “The optimal technique would be to remove all particle-bound water but no ammonium nitrate or semivolatile organic PM.”

This is effectively treated as axiomatic, as a given that requires no serious justification. The fact that

2-52/7 “Particle-bound water is not included in the mass of PM subject to regulation and

control”
provides no more than a circular justification; why is it excluded from the regulatory definition?

The claim that

2-51/25 “Since water is not a pollutant, it is necessary to remove most of the particle-bound water before weighing”

seems equally circular; in a droplet of sulfuric acid, why should only the sulfate be considered a pollutant?

The document needs a better articulation and synthesis of the considerations favoring and opposing the inclusion of particle-bound water in the definition of PM. Sampling PM so as to minimize the contribution of water brings real benefits in terms of the reproducibility and interpretability of common measurement techniques. However it also carries real costs in terms of sample integrity and the relevance of measurements to ambient exposures. The benefits may well outweigh the costs, but the reader should be led to that judgment by a careful and impartial examination of the issue. With an accurate understanding of why we now try to dry sampled particles, we will be better positioned to evaluate novel measurement methods that may arise in the future.

I think the main reason we now try to minimize particle-bound water is the historically contingent one that some years back we established laboratory weighing of filters as the reference method of measurement. Water vapor does differ from ammonium nitrate and semivolatile organics vapors in being ubiquitous and variable in indoor air. Specified laboratory limits aren’t necessary for ammonium nitrate and organics vapors, as these should be negligible anyway, but natural variations in relative humidity are unacceptably large and must be controlled if measurement outcomes are to be reproducible. In principle, mass at ambient conditions could be approximated by equilibrating each individual sample in the lab to the ambient humidity at which it was collected. In practice, it is obviously very much easier to re-equilibrate all samples to a standard humidity. On this interpretation, then, samples are equilibrated at 30-40% humidity not because that condition is necessarily what we want to characterize but because that conditioning is required for reproducible results with our chosen measurement.

A second reason to minimize particle-bound water is introduced by some – but not all – of the continuous methods. As the document explains (2-33/20), these are the “continuous monitors that measure changes in mass collected on a filter over long sampling times. If particle-bound water is not removed, changes in relative humidity would cause changes in the mass of PM collected over previous hours or days. These changes could be much greater than amount of PM mass added in one hour.” This rationale for removing particle-bound water does not apply, however, to nephelometry and other instantaneous *in-situ* methods, or to filter techniques employing advancing tape media. The distinction should be acknowledged as an advantage of these methods when applied to the study of semivolatile PM components.

Removing particle-bound water thus makes gravimetric and TEOM measurements significantly more consistent. At the same time, of course, it makes these measurements less faithful to actual ambient conditions, and hard to compare with methods that are able to measure ambient mass concentrations without drying. Particle-bound water is relevant to visibility and radiative effects, to particle deposition, and to chemical transport modeling. Are there counterbalancing reasons for expecting it to be irrelevant to health effects?

The document offers no evidence that particle-bound water is less hazardous than other PM components. Water vapor and cloudwater are natural and uncontrollable, but particle-bound water is neither. At humidities below 100%, water is present as liquid only because it is “dirty”, and this “dirty” water is controllable via reduction of the “pollutant” species responsible for lowering its vapor pressure. In the vast epidemiological literature, where are the indications that dry particle mass is superior to ambient particle mass as a predictor of health effects? I don’t see the issue addressed anywhere in this document’s toxicological and epidemiological chapters. It may be obvious that “water can’t hurt”, but 15 years ago it was obvious that 15 $\mu\text{g}/\text{m}^3$ of fine particles could not cause mortality. As for water’s being “natural”, so is most coarse PM but we still monitor it.

The health-effects chapters need to explicitly address the biological implications of removing particle-bound water and the species unstable in its absence. The document acknowledges the problem that removing particle-bound water generally causes additional losses of ammonium nitrate and semivolatile organics. It notes that

2-31/29 “The aqueous solutions also may act as a carrier to convey soluble toxic species to the gas-exchange regions of the respiratory system, including species that would be removed by deposition in the upper airways if the particles had remained in the gas phase ...”

But I see no discussion weighing the methodological benefits of drying PM against the costs of overlooking possible health insults that depend on the aqueous phase.

These are comments on the PM Criteria Document, not an argument for changing the FRM. All I am looking for is just a clearer recognition and airing of the issues for future reference, particularly

- a) the centrality of particle-bound water and the broad ramifications of the decision to exclude it from the definition of PM;
- b) the fact that excluding particle-bound water *is* a decision, one that could be made differently given new measurement techniques or new health findings;
- c) the recognition that this decision should involve the health-effects community in addition to measurement specialists.

To give “water is not a pollutant” as the reason for removing particle-bound water today is to risk establishing a dogma that will constrain thinking five years from now. (Five CAA years, of course ... maybe eight or nine calendar ones!)

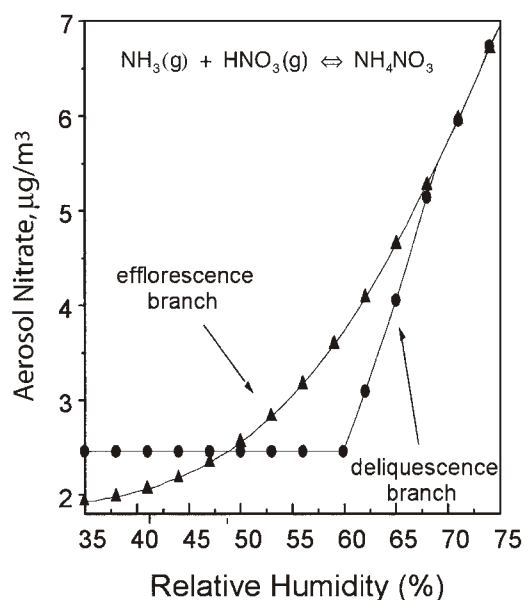
The synthesis in Chapter 9 will obviously need to integrate the dosimetric, toxicologic, and epidemiologic materials from Chapters 6-8. However, it must also address the health-effects implications of the following messages from Chapters 2-4.

1. "What you see is what you breathe." That is, hazy conditions at midday (when relative humidity is lowest) are a visible sign of elevated $PM_{2.5}$ levels.

Relevance: If there is a health basis for a $PM_{2.5}$ NAAQS, then there are scientifically sound reasons to educate people to interpret limited visual range as a health advisory

2. Health-effects researchers have an interest in particle-bound water. Modifying PM to remove bound water necessitates the loss of dissolved species that are unambiguously anthropogenic and controllable, as illustrated below by Figure 3.6 of the NARSTO PM Assessment.

CHAPTER 3



Relevance: The potential contributions of ammonium nitrate and semi-volatile organics to health effects should figure explicitly in decisions to dry or otherwise modify PM samples.

FIGURE AT LEFT: at fixed concentrations of ambient ammonia and nitric acid, particulate ammonium nitrate concentrations depend strongly on ambient humidity (and, hence, on particle-bound water content)..

Figure 3.6. Predicted particulate nitrate concentration as a function of relative humidity for a typical environment. The actual value in the atmosphere will depend on the history of the aerosol particles.

3. The distinction between policy-relevant background and controllable anthropogenic PM can be difficult to quantify in individual air samples.

Relevance: Assessments of episodic risk from controllable PM carry substantially more uncertainty than do assessments of annual risk from total PM.

Background PM

Warren White, 8/23/03

references are to page/line

The new section (3.3.3) on policy-relevant background concentrations is a helpful addition to this document. It gives a clear account of the issues that plague all estimates of background, and is refreshingly candid in its assessment:

3-103/16 “Because the concentration of PRB is so poorly quantified, ... estimates of policy relevant background concentrations will remain highly uncertain.”

Although I think the existing estimates descended from John Trijonis are likely to be low, I don’t quarrel with the conclusion that

E-10/10 “Recent but limited information about policy-relevant background concentrations and 3-104/3 have not provided sufficient evidence to warrant any changes in estimates of the annual average background concentrations given in the 1996 PM AQCD.”

I do have some additional caveats to offer, however, along with a suggestion that we seek to reformulate the problem the section is addressing.

Most of my caveats concern the danger of looking for background levels in the lowest observed concentrations. We clearly can take little assurance from the fact that

3-82/19 “Values in the lowest 5th percentile annual mean PM_{2.5} concentrations for specific sites in the AIRS data base ... [are] consistent with the range of annual mean concentrations at IMPROVE network sites in the in the western United States”

If the 5th percentile weren’t consistent, then perhaps the 1st or 10th percentile would be! Within the IMPROVE data, we can fool ourselves if

3E-1/16 “..we are interested in characterizing data obtained at the sites with lowest concentrations.”

Appendix 3E therefore needs to document the selection method by which

3E-1/16 “Only those sites in which anthropogenic sources do not contribute extensively to the observations are considered.”

A striking feature of the selection is that most sites are above 40°N latitude, and the few to the south are all west of the main impacts from the 1998 Yucatan fires noted at 3-86/15. If such smoke from Central America and southern Mexico is considered a component of PRB, as 3-89/28 indicates it is, then it is a component the site selection is biased against.

More generally, claims to have established bounds for PRB must be understood to apply only to the sites selected for study.

3-90/23 “It must be recognized at the outset that these concentrations [observed at several RRMS in the West] will only provide upper limits.”

3-103/3 “Data obtained at relatively remote monitoring sites (RRMS) in the western United States could be used to place reasonable upper limits on policy relevant background contractions.”

Actual concentrations obviously do bound the PRB at any given site. It is much less obvious that PRB in the west is indicative of PRB in the east, given the major differences in climate, vegetation, and extra-continental influences.

Finally it should be noted that, while actual concentrations necessarily bound the PRB, observed concentrations need not do so! An review of the 2001-2002 Yellowstone data, for example, shows that maximum 24h concentrations of almost 30 $\mu\text{g}/\text{m}^3$ were recorded for organic carbon in each year, about twice the maximum concentrations of 15 and 20 $\mu\text{g}/\text{m}^3$ recorded for fine mass. (And the organic mass associated with this carbon would have been greater still, perhaps 50 $\mu\text{g}/\text{m}^3$) Closer examination shows that valid mass data (from Teflon membrane filters) are lacking for the days of highest carbon (from quartz fiber filters), because the Teflon filters clogged at the unusually high loadings. The effect is hard to quantify, but major wildfires and other natural events definitely increase the risk of lost data, not only through clogged filters and power outages but also through diversion to emergency duties of Park and Forest Service personnel responsible for sample collection.

This brings us to the fact, properly highlighted in the new section, that

3-82/28 “Peak 24-h average natural background concentrations may be substantially higher than the annual or seasonal average natural background concentrations, especially within areas affected by wildfires and dust storms.”

My reading of the carbon data from Yellowstone and Bridger is that the dramatic variations in $\text{PM}_{2.5}$ mass above the 95th percentile in Figure 3E-2a,b are driven largely by vegetative fires, and are thus just as much a part of PRB as the sub 90th percentile values are. Policy-relevant background is a well defined concept, but is it a useful one in a setting such as this?

“Background” is usually understood as a single concentration value, perhaps depending on region and season, that represents a class of contributions that varies within a relatively narrow range; it is the constant term in a simple accounting model. In the case of the PM PRB, there *is*

no meaningful constant term. The Agency has elsewhere indicated that it may approach extreme events – such as wildfires, dust storms, and impacts from other continents – on an *ad hoc* basis. If episodically high PRBs are taken off the table in this manner, how sensitive are any of the Agency’s decisions to the remainder of the values?

Imagine, as a thought experiment, that we somehow knew that the observed distribution of 24h PM_{2.5} at Bridger or Yellowstone exactly represented the distribution of PRB everywhere in the country. How would the Agency make use of this information, which is much more specific than anything in immediate prospect? It would still not know the distribution of above-PRB 24h concentrations, because this depends on the unknown day-to-day correlation of background and North-American-anthropogenic components. It was for this reason that CASAC previously advised (May 23, 2002) that

“a rationale should be offered for the decision to base the rollback percentage [in the Proposed Methodology for Particulate Matter Risk Analysis] on the ‘above background’ portion of the ‘as is’ concentration distribution. The ‘background’ portion of the ‘as-is’ distribution is unknown ...”

“Natural background” is the stated goal of the Regional Haze Rules but does not figure explicitly in NAAQS considerations as I understand them. To plan implementation strategies we clearly need to understand the relationship of ambient PM to source emissions, and to develop budgets that represent this understanding, but is there any greater need to distinguish PRB from continental anthropogenic than to distinguish, say, mobile from stationary? I agree with the assessment that

3-103/5 “More definitive results for both annual average and daily average concentrations could potentially be obtained from the application of source-receptor models”,

and this approach would directly supply daily estimates for the above-PRB concentrations that are the real quantities of interest. But as section 3.3.3 also notes, such models often have more difficulty resolving natural from anthropogenic distinction than they have with some other major source distinctions. For the present, I suggest the Agency try to frame policy questions in terms that are insensitive to PRB.

Appendix 2B

Warren White, 8/24/03

references are to page/line

This is an interesting collection of background information. What is the rationale for including or excluding methods? Why is there nothing on ions, or important precursor gases such as NH₃?

Section 2B.1 surveys a number of different analytical techniques for inorganic elements, focusing largely on their potential sensitivity. It would be helpful to expand this review to a more systematic comparison of the requirements they place on sample collection. What substrates are they compatible with? How wide a range of loadings can they tolerate in routine operation? Is extraction or digestion of the sample/filter required? Can they accept uneven

deposits, or a range of deposit sizes?

The paragraph from 2B-5/24 to 2B-6/6 describes a set of source apportionment results obtained with AAAS, and sheds no light on the method itself. The sample preparation requirements for ICP-MS are not mentioned, and the comment (2B-7/1) that “Intercomparison studies are needed to establish the comparability of ICP-MS with *other* non-destructive filter analyses methods” (emphasis added) gives the impression that ICP-MS is non-destructive. The results given for SEM are uninformative.

Section 2B.2 is a worthwhile overview and discussion of the carbon measurement issues, and represents a real step forward for the Agency. However, the discussion of black carbon on page 2B-16 needs to clarify that any inference of carbon concentrations from absorption measurements rests on an assumed absorption cross-section for EC. The “similarity” of EC and BC may be an empirical fact for most existing atmospheric samples, but not by definition as line 17 indicates. A statement such as (lines 29-30) “Compared to the thermal method, the integrating sphere overestimated the BC mass concentrations by 21%” is meaningless: one measurement is chemical, the other optical, and if the optical “overestimates” the chemical measurement it is because the wrong cross-section was used for the conversion between them.

Section 2B3.1 should start out by identifying and reviewing the generic issues cited cryptically in the discussion of the beta-gauge (2B-19/26-7). Moreover, what is the dividing line between this section and section 2.2.3.3?

The TEOM discussion is unclear. For starters, I don’t think the principle of the method is ever described anywhere in the document: “tapered element oscillating microbalance” is suggestive, but not wholly self-explanatory. It is misleading to say (2B-17/31) that it does not “require” equilibration of the samples. And its different designations for PM_{10} and $PM_{2.5}$ need explicit noting so that the reader is not jarred by “Thus, the TEOM does not provide data equivalent to the FRM” [for $PM_{2.5}$] (2B-18/4) just a few lines after “the designation of the TEOM as an equivalent method for PM_{10} ” (2B17/28).

Miscellaneous details

Warren White, 8/31/03

references are to page/line

The treatment of particle size fractions in Section 2.1.2.2 is very good. I appreciate the responsiveness to my comments on draft 3.

2-98/29: Should read “The two NETWORKS also differ in their correction for positive artifacts”.

2-100/20: “Analytical techniques exist for ... elements (except carbon)”
How about oxygen?

Table 3.3 and Table 9.3: The value of 535 ng/m³ for coarse-particle Si in both tables appears to be a typo – if correct, it is stunningly unrepresentative at less than one-third the value for Al.

4-92/1: “According to this expression, a clean atmosphere would have a turbidity value of 1.” This implies, presumably unintentionally, that the Agency considers water vapor and all particles to be “dirty”.

4-154/21-5: “Visibility is an effect ...” should be changed to “Haze is an effect of suspended particles. Therefore, visibility impairment may be controlled ...”

4-158/2-6: Should read “The magnitude of the Rayleigh scattering depends on gas density and wavelength. For simplicity, a standard value of 10 Mm⁻¹ is often employed (Malm, 2000).”

4-158/15: Who says soot is primarily from FOSSIL fuels? See page 4-92, line 25!

4-167/16-7: Delete “and the threshold contrast is 2% of the extinction coefficient”

4-167/21-2: Should read “where visual range is in kilometers and b_{ext} is in km⁻¹. If a threshold contrast of 2% is assumed, the coefficient K is 3.912.”

Dr. George T. Wolff



George T. Wolff, Ph.D.
Principal Scientist
General Motors Corporation
Public Policy Center
MC 482-C27-B76
300 Renaissance Center
Detroit, Michigan 48265-3000

Phone: 313-665-2948
Fax: 313-665-0746
Email: george.wolff@gm.com

August 20, 2003

Comments on PM Criteria Document (4th draft)

by

George T. Wolff

Chapter 1

p. 1-17, line 52 – Please remove the S from my name.

Chapter 3

1. p. 3-7, Figure 3-1a & b – These figures are very difficult to read. I even printed a copy from the CD and it was only marginally better than the one mailed to me.
2. p. 3-8, lines 8-9 – This incorrectly characterizes the trends in Figure 3-2. Except for rural sites, there was a plateau from 1996 to 1999, but since then the decreasing trend has resumed and the 2001 levels are the lowest ever.
3. p. 3-10, figures 3-4a & b – These figures are unreadable. One of the cut points should be 15 so the extent of nonattainment can be seen.
4. p. 3-16 to 3-17 – Put a line on figure 3-7 indicating the annual NAAQS.

5. P 3-35 – Units for PM2.5 and PM10-2.5 are erroneously labeled ng/m3 in Table 3-2. Same for Table 3-3.

6. P 3-84, figure 3-22 – What is plotted – PM2.5 or PM10?

7. p 3-100, line 3 – I disagree. See comment 2 above.

Chapter 4

p. 4-157, line 8 – Change “nitrogen oxide” to “nitric oxide.”

p. 4-206 line 21 – I would also add the reference: National Research Council (2001), “Climate Change Science An Analysis of Some Key Questions.”

p. 4-206, line 31 to p. 4-207, line 3 – I would eliminate this. Since the TAR was completed, there have been about a half-dozen papers published refuting the ENSO claim made in the TAR.

p. 4-207, line 10 – Change “indicate” to “suggest.”

P 4-207, line 12 – Change “This is expected” to “The IPCC expects this.”

p. 4-207, line 12 – Change “These changes will” to “Such changes could.”

p. 4-207, lines 16 & 17. Change to read: “The IPCC TAR expects wide variations.....” Delete “can be expected.”

p. 4-207, lines 17 & 18 – Change to read: “In general, the IPCC expects the projected climate change impacts to represent.....”

p. 4-207, line 24 – Change to read: “change, the IPCC identifies some climate change impacts that may be locally.....”

p. 4-208, lines 2-5 – I recommend deleting this sentence and all the references because they are all based on the flawed modeling scenarios contained in the US Assessment report.

p. 4-208, line 6 – Insert “somewhat” before “successful.”

p. 4-208, line 24 – Insert “by scattering” after “reduction.”

p. 4-211, line 1 – Insert “water vapor” before “carbon dioxide.”

p. 4-211, line 4 – Delete the Schneider, 1992 reference.

p. 4-211, lines 10 to 15 – A reference is needed here. I never heard this before.

p. 4-212, line 18 – It should be stated that everywhere else in the CD black carbon is called elemental carbon.

p. 4-416, line 3 – Not just biofuels but coal as well.

P 4-217, line 13 – Figure 4-41???

p.4-217, lines 18-24 – Delete. Parts of this are wrong and it is not relevant.

p. 4-238, lines 13-15 - What is the basis of this statement? I cannot find a discussion of this point anywhere in section 4.5.

Chapter 6

I did not read this chapter, but I searched it for something that the Panel requested to be included at the last meeting and in our September 30, 2002 letter to the Administrator. We requested that examples of the magnitude of the deposited and retained doses resulting from environmental exposures to PM be added. Has this been added? I could not find it.

Chapter 8

Time Series Studies

While it is true that most recent PM_{2.5} and PM₁₀ studies found significant associations with mortality, many did not include other pollutants. It is also true that most studies that included other criteria pollutants and/or PM_{10-2.5} found equal to or stronger associations between mortality and a pollutant other than PM_{2.5} or PM₁₀. It is also clear that there are a number of studies that find no significant associations.

There are now a sufficient number of studies that allows one to cherry-pick a subset of studies to implicate any of the criteria pollutant or PM_{10-2.5}. EPA has emphasizes the ones that implicate PM_{2.5}

To further add to the uncertainty of the time-series results, a couple of issues have re-surfaced which had been thought to have been put to rest: model specificity and control for weather. In their commentary on the revised GAM analysis, the HEI special review panel wrote: “Neither the appropriate degree of control for time in these time-series analyses, nor the appropriate specification of the effects of weather, has been determined. This awareness introduces an element of uncertainty into the time-series studies that has not been widely appreciated previously. At this time, in the absence of adequate biological understanding of the time course of PM and weather effects and their interactions, the Panel recommends exploration of the sensitivity of these studies to a wider range of alternative degrees of smoothing and to alternative specifications of weather variable in time-series models.”

In my opinion, these statements are questioning the validity of all of the time-series studies, and point out our lack of knowledge concerning a biological mechanism.

Long-term Studies

There are really only four cohort data sets: the 6 city, ACS, AHSMOG, and the veterans studies. The first two show a PM relationship, the last two show none. The authors of chapter 8 dismiss the latter two and accept the first two as being correct, but fail to provide sound scientific reasons for doing this.

In addition, there are a number of findings in the first two studies that cast doubt on the validity of the results that the authors either do not mention or downplay their significance. The first is a lack of an association between PM and respiratory disease (such an association is seen in many of the time-series studies). The second is that there is no statistically significant PM-mortality effect in 34% of the 6-city cohort and in 59% of the ACS cohort who have more than a high school education. This indicates that some socio-economic confounder is missing. Another is that SO₂ is implicated as being as important as PM in determining mortality in the ACS study. Given the low ambient concentrations of SO₂ and the even lower indoor concentrations, this seems like an implausible finding. Another is the ACS finding that prior disease is protective. When risks in ACS were estimated by prior disease status, they found that those with no disease tended to die 4 years earlier than those with prior disease. This is contrary to logic.

In light of these findings, it seems there are fewer reasons to doubt the validity of the AHSMOG and Veterans findings than the other two.

Chapter 9 and the Executive Summary

Any pretense of concern over uncertainties discussed in previous chapters is abandoned in Chapter 9 and the Executive Summary. The authors present a compelling case implicating PM to numerous health endpoints. They do this by citing only those studies (or parts of them), and in many cases overstating them that support their position.

Appendix B – Roster of the CASAC Particulate Matter Review Panel

**U.S. Environmental Protection Agency (EPA)
Science Advisory Board (SAB) Staff Office
Clean Air Scientific Advisory Committee (CASAC)
CASAC Particulate Matter Review Panel***

CHAIR

Dr. Philip Hopke, Bayard D. Clarkson Distinguished Professor, Department of Chemical Engineering, Clarkson University, Potsdam, NY

Also Member: Research Strategies Advisory Committee
Executive Committee

CASAC MEMBERS

Dr. Frederick J. Miller, Vice President for Research, CIIT Centers for Health Research, Research Triangle Park, NC

Mr. Richard L. Poirot, Environmental Analyst, Air Pollution Control Division, Department of Environmental Conservation, Vermont Agency of Natural Resources, Waterbury, VT

Dr. Frank Speizer, Edward Kass Professor of Medicine, Channing Laboratory, Harvard Medical School, Boston, MA

Dr. George E. Taylor, Jr., Professor and Assistant Dean, School of Computational Sciences, George Mason University, Fairfax, VA

Dr. Sverre Vedal, Professor of Medicine, National Jewish Medical and Research Center, Denver, CO,

Dr. Barbara Zielinska, Research Professor, Division of Atmospheric Science, Desert Research Institute, Reno, NV

CONSULTANTS

Dr. Jane Q. Koenig, Professor, Department of Environmental Health, School of Public Health and Community Medicine, University of Washington, Seattle, WA

Dr. Petros Koutrakis, Professor of Environmental Science, Environmental Health, School of Public Health, Harvard University (HSPH), Boston, MA

Dr. Allan Legge, President, Biosphere Solutions, Calgary, Alberta

Dr. Paul J. Liroy, Associate Director and Professor, Environmental and Occupational Health Sciences Institute, UMDNJ - Robert Wood Johnson Medical School, NJ

Dr. Morton Lippmann, Professor, Nelson Institute of Environmental Medicine, New York University School of Medicine, Tuxedo, NY

Dr. Joe Mauderly, Vice President, Senior Scientist, and Director, National Environmental Respiratory Center, Lovelace Respiratory Research Institute, Albuquerque, NM

Dr. Roger O. McClellan, Consultant, Albuquerque, NM

Dr. Gunter Oberdorster, Professor of Toxicology, Department of Environmental Medicine, School of Medicine and Dentistry, University of Rochester, Rochester, NY

Dr. Robert D. Rowe, President, Stratus Consulting, Inc., Boulder, CO

Dr. Jonathan M. Samet, Professor and Chair, Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

Mr. Ronald White, Research Scientist, Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

Dr. Warren H. White, Visiting Professor, Crocker Nuclear Laboratory, University of California - Davis, Davis, CA

Dr. George T. Wolff, Principal Scientist, General Motors Corporation, Detroit, MI

SCIENCE ADVISORY BOARD STAFF

Mr. Fred Butterfield, CASAC Designated Federal Officer, 1200 Pennsylvania Avenue, NW, Washington, DC, 20460, Phone: 202-564-4561, Fax: 202-501-0582, (butterfield.fred@epa.gov)

* Members of this SAB Panel consist of:

a. SAB Members: Experts appointed by the Administrator to serve on one of the SAB Standing Committees; and

b. SAB Consultants: Experts appointed by the SAB Staff Director to a one-year term to serve on ad hoc Panels formed to address a particular issue.

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